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Evaluating cholesterol screening in a community pharmacy

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ABSTRACT

The purpose of this research project was to evaluate the role of the community pharmacist in screening, identifying, and referring ambulatory patients with high total blood cholesterol (TBC) in a community pharmacy. Fifty seven patients, out of 241 initially screened individuals, met the study inclusion criteria and were accepted into this study. Of these 57 patients, 51 patients completed the six month study period. The normal population group consisted of 164 participants with TBC < 200 mg/dL at the initial cholesterol testing (visit 1). The drop out group represented six patients who failed to continue attending the two follow up tests (visit 2 and 3). For screening purposes, a non-fasting whole blood sample was used to measure TBC using the Boehringer Mannheim Reflotron analyzer.

The project was evaluated based on mean TBC levels obtained during the initial screening and the two follow up tests, pre-test and post-test scores, behavior and lifestyle changes, and the number of patients who received a physician's order for lipid analysis as a result of initial screening results. In addition, influence of age and educational background on lowering TBC in visits 2 and 3, patient acceptance of blood screening in a community pharmacy and willingness to pay for this service in the future were also determined.

To assess the level of significance among the means of the tested parameters, both parametric (one-way analysis of variance, Scheffe's post hoc test and two sample t-test) and non-parametric statistics (Mann-Whitney and chi-square test) were used at a probability level of less than 0.05. There was a significant difference in mean TBC levels between visit 1 and 2, and between visit 1 and 3 ($P< 0.01$). However, no statistically significant difference was found between visit 2 and 3 ($P= 0.48$). In addition, there was no significant difference in the incidence of high blood cholesterol in terms of gender or age difference at the initial screening. Further, mean TBC levels between males and females remained statistically insignificant during the two follow up tests. However, younger patients were able to lower their mean TBC level in visit 2 and 3 compared with older patients ($P=< 0.031$). The one-way analysis of variance results showed that there was no statistically significant difference in TBC changes during the three visits by subjects categorized by educational background levels. Patient's attitude toward the idea of blood test measurement in community pharmacies was positive. Ninety eight percent of the study group stated that they strongly liked such an idea, 92.16% expressed a willingness to pay an average of $4.55 (range $3 or less to $10), and all agreed that it was a convenient service for them.

It was concluded that cholesterol screening in this

community pharmacy was effective and acceptable, and may prove to be financially feasible when effectively planned and marketed. This service provides the community pharmacist with an opportunity to offer a unique patient-oriented public service.

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INTRODUCTION

Historical Background

Cardiovascular disease (CVD) is the major cause of death and disability in the United States. It accounts for more deaths than all forms of cancer combined.[1-3] Coronary heart disease (CHD) strikes about five million Americans and is the cause of 550,000 deaths in the United States yearly.[3,4] The direct and indirect cost of CVD and CHD has been estimated at $85.21 and $64.4 billion a year, respectively.[2-6] It was postulated that lowering blood cholesterol would result in direct benefits from anticipated reductions in lifetime expenditures for medical care. Indirect benefits result from an expected extension of work-life secondary to reduction in morbidity and mortality.[5]

According to the updated statement of the 1970 Inter-Society Commission for Heart Disease Resources, there has been a significant decline in CVD mortality (35-40%) that appears to be continuing to the present. This decline in CVD as well as the distinct reduction in CHD mortality has coincided with a more effective control of hypertension, cigarette smoking, and lower consumption of fat and cholesterol in the American diet.[5] It has been estimated that 60% of such decline in CHD mortality was attributed to life style changes and 40% due to medical intervention.[7] This association was attributed to environmental

influences, since genetic characteristics of a population cannot change in a short time. Pathologic and experimental observations support such association both in animal and human studies.

Broad scientific studies ascertained the association between elevated serum lipids, due to either hereditary and/or life style, and the development of atherosclerosis and associated CHD. Further, the linear relationship between plasma lipid concentration, especially cholesterol, and the severity of atherosclerosis is well established.[5,8-13] The early atherosclerotic lesions can cause significant narrowing of the blood vessels. However, this is a slowly developing process and presents no clinical symptoms in most cases. It is not until a significant occlusion of the vessel, due to calcification and fibrosis, that a clinically active period can be observed. This lesion is usually common in the fifth or sixth decade of life.[14] Variation in patient susceptibility is wide and is dependent on the type and intensity of underlying risk factors and the duration of exposure to those risk factors. It is important to keep in mind that the clinical manifestations of coronary heart disease often strike without warning. It is quite possible that the first manifestation is an irreversible brain or myocardial infarction or even sudden death. Therefore, emphasis on primary prevention is of a great importance.

Hyperlipidemia

Hyperlipidemia (HLP) is defined as an elevation of plasma lipids, namely, cholesterol, triglycerides, and phospholipids. Hyperlipoproteinemia is a disturbance of lipid transport that results from abnormalities in the synthesis or degradation of plasma lipoproteins.[10,15-19] Diverse proportions of cholesterol ester and triglycerides act as a core for high molecular weight particles called lipoproteins. In order for these particles to travel in the circulatory system, a surface coat of phospholipids, which is polar in nature, is needed. In addition to phospholipids, the polar coat contains small amounts of un-esterified cholesterol. These components represent lipoprotein (LP) particles. The outer surface of LP particles contains specific proteins, called apoproteins, which have the ability to bind to specific enzymes or transport proteins on cell membranes. Therefore, these apoproteins are of great importance in directing the lipoprotein particles to their sites of metabolism.[10,15]

There are five different classes of LP that normally circulate in human blood. They differ in their density, particle size, electrophoretic mobility, core composition, and the apoproteins in their surfaces.[18,20] The five main types are chylomicron, very low density lipoprotein (VLDL), intermediate low density lipoprotein (IDL), low density lipoprotein (LDL), and high density lipoprotein (HDL). The biochemical and clinical features of these lipoproteins are

presented in Table I.[21]

Table I:

Biochemical and Clinical Features of Lipoproteins.[1]

	Lipoprotein			
	Chylomicron	VLDL[2]	LDL[3]	HDL[4]
Composition (%)				
Cholesterol	3-7	20-30	51-58	18-25
Triglyceride	85-95	50-65	4-8	2-7
Protein	1-2	6-10	18-22	45-55
Phospholipid	3-6	15-20	18-24	26-32
Physiological origin	Intestine	Intestine and liver	VLDL catabolism	Liver and intestine
Physiological function	Transports dietary triglyceride	Transports endogenous triglyceride	Transports cholesterol to extra-hepatic cells	Transports cholesterol from extra-hepatic cell to liver
Electrophoretic mobility	Origin	Pre-beta	Beta	Alpha
Appearance in plasma after refrigeration	Cream layer at surface	Turbid	Clear	Clear
Clinical features of high level	Eruptive xanthomas; lipemia retinalis; pancreatitis; organomegaly	Glucose intolerance; hyperuricemia	Premature atherosclerosis; corneal arcus; tendious and tuberous xanthoma	No associated abnormality

[1]Adapted from Reference #18 and #21.
[2]Very low density lipoprotein.
[3]Low density lipoprotein.
[4]High density lipoprotein.

In order to understand the etiologies of the lipid disorders, CHD, and approaches to their treatment, a brief review of lipid transport and metabolism is presented.

Lipid Transport

Two pathways are involved in the transportation of lipids in our circulatory system, namely, the exogenous and the endogenous pathways.

a. Exogenous Pathway

The exogenous pathway involves the largest amount of lipoprotein which transports more than 100 grams of triglycerides and about one gram of cholesterol per day. Exogenous fat and cholesterol are incorporated within intestinal epithelial cells into a large LP called chylomicron. These particles reach the general circulation through intestinal lymph channels where they are subsequently transported to the capillaries of adipose tissues and skeletal muscle.[15] Chylomicrons are then exposed to the enzyme lipoprotein lipase (LPL) which is activated by apoprotein CII located on their surfaces. As a result, free fatty acids and monoglycerides are liberated in capillaries, where they reach adipocyte or muscle cells for subsequent oxidation or re-esterification to triglycerides.

The remainder of the chylomicron dissociates from the capillary endothelium and reenters the circulation as a remnant particle (IDL). These particles travel to the liver, where they are effectively taken up through binding

of apolipoprotein E to its specific receptors on the surface of the hepatocyte. The surface-bound remnants are then taken into the cell and then degraded within lysosomes by the process called receptor-mediated endocytosis.[15,22,23] In summary, the overall result of the chylomicron transport process is to deliver dietary triglycerides to adipose tissues and cholesterol to the liver.

b. Endogenous Pathway

Between meals, free fatty acids are usually released from adipose tissue and supplied to the liver where about 80% are used for energy. The rest of the free fatty acids are incorporated into VLDL particles along with cholesterol, phospholipids, and apolipoprotein. The VLDL particles are then secreted into the circulation. Therefore, whereas chylomicron particles carry triglycerides of dietary origin, VLDL particles carry triglycerides of endogenous origin. These later triglycerides have been formed from excess fat stored in and mobilized from adipose tissue. The VLDL particles are then exposed to the same LPL enzyme where triglycerides are removed from its core leading to smaller and denser IDL particles. These newly formed particles are metabolized and removed from the circulation by two different mechanisms. First, they may be taken up by specific receptors on the surface of the liver. Second, 50% may be converted to LDL particles via hepatic triglyceride lipase enzyme. The result of these two mechanisms is a release of

LDL particles with a very rich amount of cholesterol into the general circulation. These LDL particles transport cholesterol to peripheral cells that utilize cholesterol for cell membrane and hormonal synthesis.

Since LDL particles contain 60-70% cholesterol, inefficient removal of LDL from the circulation can result in high blood cholesterol levels. Therefore, the longer the circulation time of LDL particles, the more likely they are taken up by scavenger cells (macrophage). The scavenger cells are then converted to cholesterol-laden foam cells. It has been postulated that these macrophage cells are involved in the initial formation of the atherosclerotic lesion.[11,24]

In the presence of lecithin cholesterol acetyltransferase (LCAT), cholesterol from LDL particles is esterified to form HDL particles. These particles deliver the cholesterol ester to the liver where it is removed and degraded by bile acids. Bile acids are then secreted into the intestine to facilitate fat metabolism. Thus, it is claimed that people with high LDL levels are more likely to develop atherosclerotic lesions and subsequent CHD. On the other hand, people with high levels of HDL tend to have an enhanced ability to remove cholesterol from foam cells and, therefore, are at low risk of developing atherosclerosis.[11,25-27]

Phenotype Classification of Hyperlipidemia

The hyperlipidemias were initially classified based on

their electrophoretic lipoprotein pattern first suggested by Fredrickson and Lee.[16,28] This classification has proved to be useful in classifying familial (primary) disorders or genetic abnormalities. However, it provides little information about the etiology of the lipid disorders and no information about altered concentrations of apoproteins or HDL or alteration in enzymatic activity. The American Heart Association in 1984 suggested a classification based on an etiology that would be more practical when evaluating the patient. This new classification system consists of three general categories that focus on the cause of hyperlipidemia. It entails secondary causes such as disorders in related metabolic systems, the use of certain medications, and abnormal dietary intake and lifestyle.[15-17,29]

Brown and Goldstein[15] subdivided primary HLP into two major categories. The first category includes single-gene disorders which are transmitted by a simple recessive mechanism, while the second category includes a multifactorial disorder with complex inheritance patterns. It was stated that hyperlipidemias of type II, III, and IV are associated primarily with premature coronary artery disease, whereas profound hypertriglyceridemia of type I and V is often complicated by pancreatitis.[14] A summary of the major hyperlipoproteinemias and their phenotype-disease classification is presented in Table II.[10]

In contrast to the primary causes of HLP, the

Table II:

Major Hyperlipidemias, Their Phenotype-Disease Classification, and Clinical Manifestations.[1]

Phenotype	Occurence	Elevated Lipoprotein	Plasma Lipid Concentration (mg/dL) Chol[2]	TG[3]	Clinical Manifestation
I	Rare	Chylomicron	250-400	>2500	Hepatosplenomegaly; pancreatitis; eruptive xanthomas; onset in childhood.
IIA	Common	LDL[4]	>250	<150	Premature CHD5; tendon xanthoma; detectable in childhood.
IIB	Most Common	LDL, VLDL6	>250	150-400	Premature CHD; milder form associated with obesity or diabetes.
III	Rare	VLDL remnant	375-500	600-800	Premature CHD and peripheral vascular disease; hyperglycemia; hyperuricemia in adult.
IV	Common	VLDL	225-275	375-500	Premature CHD risk; eruptive xanthomas; hyperuricemia.
V	Rare	Chylomicron, VLDL	350-400	1700-2500	Hepatosplenomegaly; pancreatitis; eruptive xanthomas. lipemia retinalis; mainly in adults.

[1]Adapted from Reference #8 and #18.
[2]Cholesterol.
[3]Triglyceride.
[4]Coronary heart disease.
[5]Very low density lipoprotein.

secondary causes, including disease state, drug therapy, or lifestyle, are usually reversible if they were appropriately identified. In some cases, however, multifactorial inherited disorders might interact with environmental factors to produce a more serious form of lipid disorder.[8,15]

Blood Cholesterol

Cholesterol belongs to the class of compounds that is characterized by the basic steroidal carbon skeleton. It is a fat-like steroid alcohol with a structural formula $C_{27}H_{45}OH$. Cholesterol is found in animal fats and oils, in bile, blood, brain tissue, milk, egg yolk, myelin sheaths of nerve fiber, the liver, kidney, and adrenal glands. It is a precursor of bile acids and is an important component in the synthesis of steroidal hormones.[a]

In spite of the fact that liver is the major site and source of cholesterol biosynthesis, nearly all body cells have the ability to synthesize cholesterol. Blood cholesterol circulates mainly in the form of LDL (65%), VLDL (15%), and HDL (20%). Hagan, et al., reported that movement from a 30 minute supine position to the standing position caused a 9.3 % increase in total cholesterol due to hemoconcentration. However, he stated that the TC/HDL ratio was not affected by such posture changes.[30]

The blood cholesterol level is a sum of both exogenous cholesterol and saturated fats from foods we eat and cholesterol that is endogenously generated by the liver. It is under restricted biochemical and enzymatic regulation including a sensitive feed back mechanism. This mechanism responds to both the blood cholesterol level and

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[a] Dorland's Illustrated Medical Dictionary. Friel J.P. (Ed.). Twenty-Sixth Edition. W.B. Saunders Company. Philadelphia. 1981; p.261.

lipoprotein receptor number, sensitivity and integrity.[10,15,22,31] Most circulating blood cholesterol is removed by converting it to bile acids in the liver. These bile acids are returned to the liver through the enterohepatic circulation. The unabsorbed fraction is degraded in the large intestine and subsequently excreted in the feces. Blood cholesterol level is affected by the rate of lipoprotein synthesis and degradation. This process is affected by the presence of efficient or defective lipoprotein receptors both in hepatic and extrahepatic tissues. Therefore, a genetic defect in LDL receptors could result in a dramatic reduction of the LDL metabolic pathway (uptake) leading to hypercholesterolemia.[5,10,22] In such a person, a build up of circulating LDL particles may occur in spite of eating a normal or low fat, low cholesterol diet. Presence of a high level of LDL and cholesterol in the blood, especially in the presence of local intimal lesions or hypertension, can lead to deposition of these particles in large and medium arteries. In addition, high blood cholesterol may suppress the synthesis of the hepatic LDL receptors. A slow but rather progressive build up of LDL with subsequent smooth muscle proliferation is the key to the formation of atherosclerotic plaque.[2,11,24,32]

An extensive body of scientific knowledge, including epidemiologic studies and animal studies, established beyond any reasonable doubt the causal relation between

elevated blood cholesterol and CHD.[2,5,10,12,20,32-34] Yusuf, et al.,[35] summarized the results of randomized clinical trials related to lowering blood cholesterol. He stated that "... at least 22 randomized trials have evaluated reduction of cholesterol levels on a total of about 40,000 individuals." Some of these trials used drugs to lower cholesterol; in three other trials, dietary polyunsaturated fat was substituted for a saturated fat diet without changing the total fat intake. Nine studies were primary trials (where there was no evidence of CHD at the time of conducting the study) while the others were secondary trials. The author stated that the reduction in CHD was directly related to both the degree of lowering cholesterol levels and the duration of such reduction.[35] In the Framingham study, it has been estimated that a 10% reduction in blood cholesterol level is associated with a 10% reduction in CHD with treatment of less than four years duration. This effect on CHD is doubled (20% reduction) with more prolonged treatment. The risk of CHD begins to increase steeply in a curvilinear fashion above a cholesterol level of 200 mg/dL. It was estimated that this risk is fourfold in the top 10% as compared with the bottom 10% (Figure 1).[12,20,23,32] In addition, Stamler, et al., documented that this relationship is not a threshold one and is not restricted to the highest quintiles, i.e., total blood cholesterol of 221-244 and 245 mg/dL or more, "but rather is a continuously graded one that powerfully affects

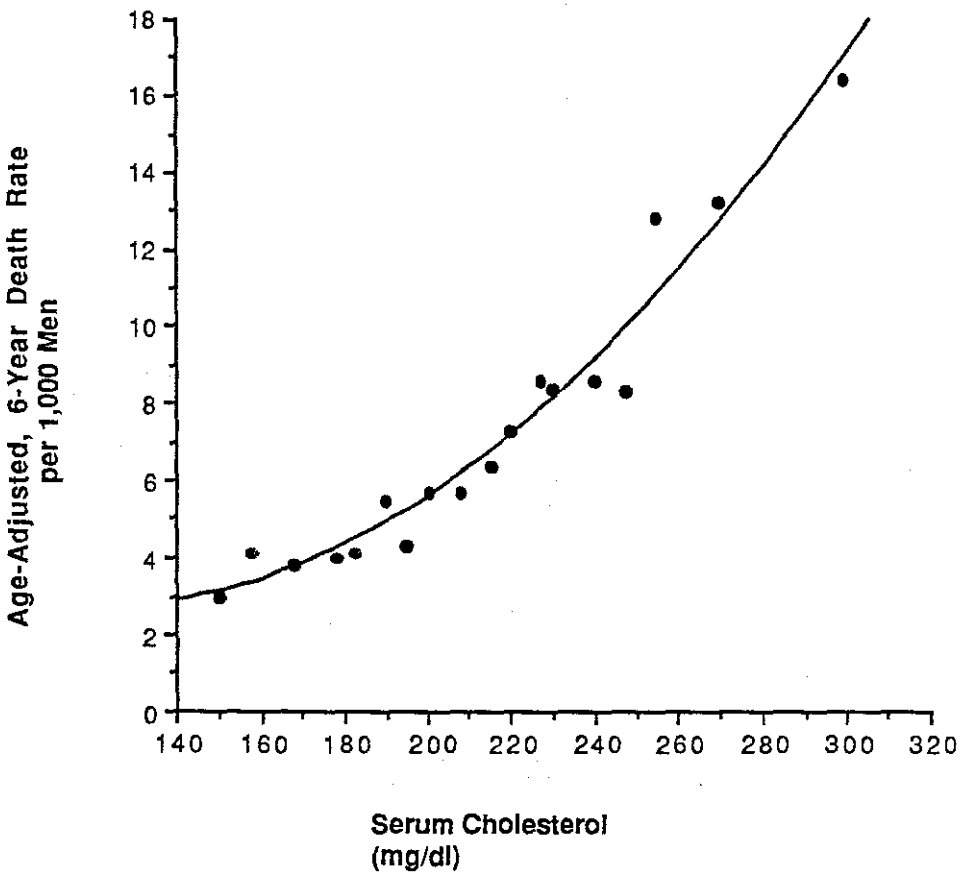


Figure 1: Relationship of Serum Cholesterol to Coronary Heart Disease Death Rate in 361, 662 Men, Age 35 - 57 During the Average Followup of Six Years (Reference #20).

risk for the great majority of middle-aged American men."[9] It was concluded, that reducing high cholesterol levels, particularly early in adult life and on a long term basis, can lead to a significant reduction in CHD.[35]

a. Effect of Dietary Cholesterol

In a typical American diet, the average amount of cholesterol consumed is 450 mg daily. The human body synthesizes sufficient amounts of cholesterol to meet its daily needs. The relative importance of dietary saturated and polyunsaturated fatty acids and cholesterol in determining the blood cholesterol level has been a controversial issue.[36] Zanni, et al., reported a considerable inter-individual heterogeneity in response to diet.[37] However, as a general rule, ingestion of a diet high in saturated fats and cholesterol results in an elevation of serum cholesterol and increases the risk of CHD.[38] This increase in serum cholesterol was reported to be linear over the entire range of the amount of cholesterol ingested. A concomitant alteration in the amount of LDL and HDL particles and the cholesterol content per particle has been documented.[26,37] It has been estimated that for each 100 mg cholesterol in 1000 Kcal of diet there is approximately 12 mg/dL increase in serum cholesterol.[36]

In an epidemiologic study, a low cholesterol level has been claimed to be associated with a higher incidence of cancer. However, it was explained that this is likely to

be due to " hypocholesterolemic effect of some cancer rather than the carcinogenic effect of lowering cholesterol level."[35] In a recent primary prevention study, it was confirmed that lowering elevated cholesterol has no influence on the cancer rate.[39,40] Another concern was the occurrence of suicidal deaths in patients with low TBC. These concerns about cancer and suicidal deaths was based on studies of alcoholics and prisoners.[41] McKenney addressed this issue and commented "No causal relationship has been demonstrated between lowering cholesterol and cancer, nor were there reports of increased cancer deaths in the two recent cholesterol lowering trials", i.e., LRC-CPPT and the Helsinki Heart study. The author added "Until lowering cholesterol has been shown to cause cancer, there is no justification for withholding cholesterol therapy on this basis."[40] With advanced knowledge of the complex nature of lipid metabolism, and application of the latest techniques of cell biology and advanced research on lipoprotein receptors, it is now clear that dietary intake of saturated fat and cholesterol does in fact affect serum cholesterol levels and lipoprotein composition.[22,26,36-38] A cholesterol/saturated fat index (CSI) has been calculated based on a modification of the regression equation computed from metabolic studies. This score enables one to determine the relative hypercholesterolemic/atherogenic potential of a given food taking into account the food's content of saturated fat and

cholesterol. It has been reported that the CSI per 1000 Kcal correlates well with mortality from ischemic heart disease (r=0.78) in men 55-64 years old from 40 countries.[42]

b. Seasonal Variation in Cholesterol Level

Several studies have conveyed the impression that cholesterol levels exhibit significant seasonal variation while others were unable to demonstrate significant variation.[4,44-47] Since serial and periodic cholesterol determination over several years has not been studied, these speculations need further investigation. In addition, some of the previous studies had limited statistical analysis of the results, and some based conclusions on results which were not statistically significant.[44]

The Lipid Research Clinics (LRC) Coronary Primary Prevention Trial (CPPT) is one well designed study that described such cyclic seasonal variation in cholesterol levels. A cohort of 1446 hypercholesterolemic 35 to 59-year-old men, initially free of CHD symptoms, were studied. This study used a uniform method for measuring blood cholesterol in the 12 LRC centers. All participants were maintained on a standard diet and were examined bimonthly for 7-10 years for cholesterol levels, body weight, and semiannual dietary assessment.[1,44] A highly significant seasonal effect in serum cholesterol level was found, with an average decrease of 7.4 mg/dL December 30 compared to

that of June 30.[1,44-47] Such a trend in cholesterol variation was observed among the 12 LRC centers that include completely different climates. Gordon, et al.,[45] pointed out that the magnitude of this seasonal variation was independent of baseline cholesterol levels as well as weight and saturated fat and cholesterol intake. Another study examined the effect of season on fasting plasma cholesterol in a group of 80 people seen during spring to autumn and another group of 73 subjects seen in summer and winter. In this study, no seasonal change in cholesterol levels was observed.[48] Several factors were suggested as a possible cause of such seasonal variation. These may include diet, temperature, exercise, duration of daylight, and intrinsic and biological rhythm. However, the etiology and mechanisms for such seasonal patterns or the role of suggested causal factors remain to be answered.[45,47]

This seasonal fluctuation in serum cholesterol is probably of minor importance in terms of the clinical management of hyperlipidemia. Serum cholesterol was reported to vary about 15 mg/dL from one visit to another and between different laboratories due to lack of standardization method between laboratories. Furthermore, a wide variety of parameters beside season of the year may affect serum cholesterol. Diet, temperature, and physical activity all are affected, in different ways, by season for different individuals. It is important, however, to take into account such trends in serum cholesterol and to be

aware of its possible existence when interpreting patient values.

Secondary Hyperlipidemia

A number of risk factors have been reported to be strongly associated with a high incidence of CHD.[2,5,10,11,32,49] Among these factors elevated blood cholesterol, high blood pressure, and cigarette smoking are the most clearly established.[5,7,50-52] In fact, elevated serum cholesterol is a powerful independent risk factor for CHD.[49,53] With the exception of familial HLP, the three well established risk factors are considered to be modifiable factors, i.e., under the patient's control. These are the areas suggested as the target in preventive medical care. Menotti, et al.,[50] reported that these three risk factors apparently "...are of universal value within almost any population group or sample" based upon the 1984 report of Inter-Society Commission.

Secondary hyperlipidemia may not only be due to ingestion of high amounts of saturated fat and cholesterol but also could be due to a pre-existing disease state and/or as a side effect of the use of drugs.[5,10,15,20,21,25,34,49] The most frequently reported forms of secondary hyperlipidemia were found to occur in association with cigarette smoking, diabetes mellitus, alcohol consumption, and ingestion of oral contraceptives. Additional disease states that might affect serum lipoprotein include Cushing's syndrome, hypothyroidism,

anorexia nervosa, uremia, nephrotic syndrome, primary biliary cirrhosis, acute hepatitis, lupus erythematosus, and monoclonal gammopathesis. Acute emotional stress, as in extensive burns, myocardial infarction, or gram negative sepsis, can also cause lipoprotein abnormalities.[10,15]

a. Cigarette Smoking

Cigarette smoking in the United States is reported to be responsible for about 30% of all deaths from CHD particularly in younger smokers. It has been reported that cigarette smokers have a 70% higher mortality from CHD compared to nonsmokers. This results in an estimated $19 billion earning loss yearly.[5,10,51] Cigarette smoking is one of the major, graded, and independent factors for CHD. The risk is even higher in smokers who also have high blood pressure, elevated blood cholesterol, and in women who are using oral contraceptives.[5,51,54]

Among the CHD risk factors, cigarette smoking is the most reported preventable cause of CHD deaths in both men and women.[10,51] The risk is proportional to the number of cigarettes smoked per day, not the number of years a person had been smoking.[4,5,10,21] Smoking is also associated with substantial lowering of HDL level, although smokers who quit smoking for more than one year seem to have HDL levels equivalent to or slightly higher than those who had never smoked.[4,10,21]

Smokers were reported to be at a significantly higher risk of stroke, even after taking age and hypertension into

consideration. As with CHD, the risk of stroke increases as the number of cigarettes smoked increases.[55,56] Cessation of cigarette smoking for two years reduces the risk of stroke, which was found to return back to the same level of nonsmokers five years after quitting smoking.[55]

Deanfield, et al.,[54] examined the effect of smoking a single cigarette followed by exercise on regional myocardial perfusion in 13 chronic smokers with typical angina pectoris. Cigarette smoking was reported to be associated with a profound silent disturbance of regional myocardial perfusion and impaired coronary blood supply in response to exercise compared with the control (16 healthy nonsmokers).[54]

Cigarette smoking, in addition to predisposing the individual to lung cancer and emphysema, was reported to transiently increase platelet aggregation, increase heart rate and blood pressure, predispose the heart to ventricular fibrillation, decrease oxygen carrying capacity of hemoglobin, and raise fatty acid levels.[5,21] Therefore, smokers tend to have lower HDL, and are more susceptible to developing atherosclerosis and CHD particularly in female smokers.

b. Oral Contraceptives

Commercially available oral contraceptives contain variable amounts of estrogen and/or progestin, both of which seem to alter the lipid profile.[10,15,57,58] It has been shown that plasma triglycerides and VLDL levels were higher

in a majority of OC users compared to nonusers.[6,10,15] However, it seems that these two active ingredients have different effects on the LDL and HDL component of blood lipids and this difference appears to be dose-related. Preparations containing low amounts of estrogen and medium to high amounts of progestin appear to cause an increase in LDL and a decrease in HDL. On the other hand, administration of conjugated estrogens significantly increases HDL.[6,57,59] Premenopausal women who used oral contraceptive products which are high in estrogen content but low in the amount of progestin had higher levels of HDL. In contrast, postmenopausal women who used estrogen had lower LDL concentrations compared to postmenopausal nonuser controls.[5,58,59]

In women with a genetic disorder, plasma VLDL levels increase dramatically when estrogen containing medications were used. Therefore, it has been recommended that plasma cholesterol and triglyceride levels be measured before the institution of oral contraceptives. Documented findings of hyperlipidemia may be considered a contraindication to the use of these drugs.[15]

c. Alcohol Consumption

Several studies have addressed the effects of moderate and severe alcohol intake on serum lipids and its association with coronary heart disease.[60-62] Ethyl alcohol consumption can produce a mild to severe elevation of VLDL fraction which appears to be dose related.[5,15,61] Ethanol

elevates the plasma triglycerides through inhibition of fatty acid oxidation and by enhancing their hepatic synthesis.[15] Chronic ingestion of large amounts of alcohol may lead to pancreatitis, eruptive xanthomas, increased blood pressure, and lipemia retinalis, especially in patients with Type IV hyperlipidemia.[6,15,62] It has been demonstrated that moderate alcohol ingestion can lead to a significant increase in HDL concentration and HDL_3 subfraction without affecting HDL mass. However, these changes were significantly decreased when ethyl alcohol was avoided.[60] It is important to point out that elevation of HDL_2 subfraction and HDL appear to be negatively associated with CHD, while more dense HDL_3 subfraction is reportedly unrelated to CHD.[60,63,64] Moderate alcohol ingestion (30 grams/day) was found to be associated with a significant rise in HDL_3 and no change in HDL_2, whereas high doses (60 grams/day) were associated with a significant rise in HDL_3 and HDL_2 subfractions.[61,63] The observed increase of HDL_2 and reduction of LDL levels in Taskinen's study[61] as well as in animal models[63] was explained by an increase in lipoprotein lipase activity (LPL). Enhanced LPL activity will in turn increase both HDL_2 and HDL_3 subfraction only in chronic alcoholics but not in moderate alcoholics. In the animal model, lecithin cholesterol acetyltransferase was addressed to be the key enzyme that is affected by alcohol dose. The enzyme activity was increased with consumption of 12% calories from ethyl alcohol but

diminished and markedly lowered with consumption of 18% and 24%, respectively.[63] In a prospective study, moderate alcohol consumption in middle aged female nurses was associated with decreased risks of CHD and ischemic stroke but was reported to increase the risk of subarachnoid hemorrhage.[65] It appears that no single pathophysiologic mechanism can explain all alcohol-induced changes in serum lipids. Alcohol consumption especially in excessive amounts may increase the risk of hypertension, stroke, cancer, pancreatitis, and liver disease. The dangers of acute and chronic excess alcohol consumption far outweigh any possible or theoretical benefits from alcohol induced elevated HDL or lowered LDL. Therefore, alcohol should not be recommended as part of any health program in the prevention of CHD.[5]

d. Obesity and Physical Inactivity as Risk Factors

In obese people, the liver tends to increase the rate of uptake of fats and carbohydrates from the intestine and to increase mobilization of fat from adipose tissue. This high load of free fatty acids may activate increased synthesis of VLDL, stimulate lipoprotein lipase activity, reduce HDL level and increase LDL level.[5,6] Although its contribution as an independent risk factor in CHD was not well established, obesity causes an alteration in many CHD risk factors. Obesity has been found to be highly associated with hypertension, glucose intolerance, and an abnormal lipid profile. Thus, extreme obesity (more than

30% over ideal body weight) is considered a risk factor and an important contributor to the risk of atherosclerosis and CHD.[5,21,25,51,64] On the other hand, Leon, et al., showed supporting evidence of the hypothesis that CHD and overall mortality are inversely related to regular physical exertion even in people with a high risk for CHD.[66] Regular exercise activity was proved to be useful in increasing the body's aerobic power, lowering heart rate and blood pressure, raising HDL concentration, reducing serum triglycerides, and decreasing body fat.[5,35] Although its beneficial impact on CHD appears to be less than those of the major risk factors, regular exercise is likely to be beneficial as part of a comprehensive risk reduction program.[5,35]

e. High Blood Pressure

Elevated blood pressure is directly related to the risk of every major cardiovascular disease. It is more prevalent among blacks, elderly, obese, and oral contraceptive users. It has been reported that either elevated systolic or diastolic pressure increases the risk of CHD, although systolic pressure may be a better predictor.[5,10,21,35,67] High blood pressure has been found to be a more reliable CHD predictor than the level of cholesterol or cigarette smoking.[21] The Framingham study documented the poor correlation between blood cholesterol level and blood pressure ($r=0.12$).[67] However, a powerful interaction was found to exist between high blood pressure

and elevated blood cholesterol to produce CHD. The higher the blood pressure, the greater the probability of stroke and CHD. Serum cholesterol was found to be a strong and graded risk factor over its entire distribution from 182 mg/dL and higher in men with high blood pressure.[10,68] Further, it has been addressed that the risk of CHD mortality at least doubled in hypertensive males who smoke cigarettes.[68] Several techniques were suggested to control elevated blood pressure, including weight reduction, salt and caloric restriction, physical exercise, stress reduction, and selecting antihypertensive medications with minimal or no adverse effects on serum lipids.[51,67]

f. Diabetes Mellitus

Diabetes is a metabolic syndrome characterized by symptomatic glucose intolerance. It is more prevalent in females (2/3) than in males (1/3). Insulin-dependent diabetics represent about 5-10% of the 4-5 million diabetic population in the U.S.A.[18] Insulin is an important substance in blood glucose regulation. Low insulin level or lack of its secretion causes an increase in blood glucose due to decreased tissue utilization and increased fat mobilization from adipose tissue. As a result, a significant increase in VLDL and chylomicron synthesis and secretion in susceptible persons may occur. In some patients, there may be a slower rate of VLDL catabolism.

Controlling blood sugar by either diet, weight loss, or drugs can reverse these abnormal lipid profiles. However,

a depressed HDL in patients with non-insulin dependent diabetes mellitus may not be corrected by controlling blood glucose.[6] Uncontrolled diabetes, on the other hand, has been found to be associated with vascular disease and increased risk of developing CHD.[21] Males with glucose intolerance have about a 50% higher chance of developing coronary artery disease (CAD) compared to males with no glucose intolerance. This effect varies widely based on glucose level and the coexistence of other risk factors. The lower the number of risk factors, the lower the risk of CHD. Diabetic females were reported to have double the risk of developing CAD than diabetic males, even when considering the CAD rate difference between males and females. It is important to remember that both hyperlipidemia and hyperglycemia tend to be associated with obesity and hypertension.[5,21]

Diabetics are more prone to a rapid progression of cardiovascular disease including hypertension, congestive heart failure, and CHD.[18] Atherosclerotic disease is still considered the major cause of death in 75% of all North American diabetics. It has been postulated that this high death rate is due to microvascular and neuropathic complications that lead to an extension of the atherosclerotic process and subsequent peripheral vascular disease.[5,18] These cardiovascular consequences of uncontrolled blood glucose may depend on the level of insulin, age of onset, etiology of the disease state, or

adequacy and efficacy of nutritional and drug therapy.[5]

g. Drug-Induced Hyperlipidemia

Several studies have reported evidence of drug-induced hyperlipidemia. The most commonly reported drugs that may induce an abnormal lipid profile include: thiazide diuretics, beta blockers, nonsteroidal anti-estrogens, corticosteroids, oral contraceptives, and retinoic acid derivatives.[6,10,15,16] Allopurinol and some benzodiazepines can significantly increase triglycerides.[32] Furthermore, many studies have documented the potential adverse effects of antihypertensive medication, in particular, on blood lipids.[69-73] Thiazide diuretics were reported to consistently increase total blood cholesterol (TBC) levels by 4-13% and LDL by 7-29% compared to baseline levels. This phenomenon appears to be dose related.[6,71] Short term studies, however, have shown that the TBC/HDL ratio as well as HDL concentrations are often unchanged.[70]

Treatment with beta blockers, especially beta-1 and non-selective agents with no intrinsic sympathomimetic activity, also produce adverse effects on blood lipid profiles. This effect appears to worsen when these agents are used in combination with thiazide diuretics.[6,70] In addition, methyldopa has been reported to decrease HDL by 13-15%.[6] Among clinically used antihypertensive drugs, pindolol, acebutolol, labetolol, guanabenz, hydralazine, prazosin and calcium channel blocking agents appear to have few or no effects on serum lipids.[6,71,72] In contrast,

captopril in a dosage of 50 mg twice a day was found to be associated with beneficial effects on serum lipids. A significant reduction of 101 mg/dL in triglyceride level, 50 mg/dL decrease in TBC, and 11% increase in HDL concentrations were noticed. Interestingly, these effects disappeared when captopril was discontinued, suggesting a cause-and-effect relationship.[74] It has been concluded that captopril has no significant harmful effects on serum lipids.[57] Isotretinoin and etretinate were reported to cause a significant increase in serum triglycerides and cholesterol resulting in eruptive xanthoma and pancreatitis. The exact mechanism of such severe lipoprotein changes is unknown, although VLDL and LDL synthesis enhancement has been proposed.[6,73]

It should be remembered that treating one factor is solving part of the CHD multifactorial problem. Therefore, screening for possible CHD risk factors and taking the steps to correct them may be considered the initial step in controlling CHD.

Screening for Hyperlipidemia

In order to initiate the steps toward controlling CHD, the general public needs to be informed about the significance of elevated blood cholesterol, its relationship with CHD, and methods of prevention and treatment available. Identifying individuals who need their cholesterol controlled is a crucial step toward the control of CHD. However, hyperlipidemia rarely produces

symptoms until late in life when angina pectoris, myocardial infarction, or heart attack could be the first and the only symptom.[75] At this point, treatment may not restore the patient's original state of health but may halt further deterioration and progression or complication of coronary events. Therefore, as stated by McKenney "...using symptoms to identify patients needing treatment is not wise."[75]

For a screening program to be justified, the following criteria must be met:[7]

1. The disease or condition must have a significant effect on the quality or quantity of life.
2. Acceptable methods of treatment must be available.
3. The condition must have an asymptomatic period during which detection and treatment significantly reduce morbidity or mortality.
4. There are tests for this pre-symptomatic stage that are reliable and acceptable in terms of risk, cost, and degree of discomfort to the patients
5. Treatment in the asymptomatic phase must yield therapeutic results superior to that obtained by delaying treatment until symptoms appear.
6. Facilities are available for diagnosis and treatment of those rated positive by the screening test.

Until recently, establishing programs to screen cholesterol levels of large number of people was difficult to establish in a practical way due to the length of time and the high cost for each test. To correctly identify and subsequently treat individuals with high blood cholesterol, accurate and precise instruments are required.[76] Now, there are at least three portable analyzers available whereby blood levels of different blood components can be measured from a finger stick blood sample.[77] The technological advantages of these portable analyzers, specifically those utilizing whole blood dry chemistry reagents, have made cholesterol screening for the public a reality. In such cases, blood cholesterol levels can be measured using approximately two drops of whole blood, and the test result can be obtained in less than three minutes.

There was considerable variability between laboratories in terms of accuracy of cholesterol measurement.[10,20,78,79] This situation restrained the national program intended to control heart disease. For this reason, the National Cholesterol Educational Program (NCEP) and its Laboratory Standardization Panel on Blood Cholesterol Measurement developed recommendations to improve laboratory performance. The following is a broad outline of the panel's recommendations that were addressed to improve the quality of cholesterol measurement:[76]

1. Clinical laboratories in the United States should employ uniform cholesterol cutpoints for

identifying adults at high risk for CHD.

2. Laboratories must minimize method-specific bias and also achieve adequate precision of cholesterol measurement. This includes particular attention to method/instrument and calibration procedures.

3. A deviation from the true cholesterol value of a standard sample (bias) should not exceed plus or minus 5% from the true value and should not be greater than plus or minus 3% from the true value within five years.

4. All newly available portable chemistry analyzers for cholesterol measurement need further evaluation before they are adopted for routine use with patients.

5. Proper training of technical personnel in the use, maintenance, and quality-assurance procedures are necessary.

6. All clinical laboratories' measurements in the U.S.A. should and can be standardized so that their values are traceable to the Center of Disease Control (CDC) reference method or to the National Bureau of Standards definitive method. This may be achieved by utilizing certified reference materials.

7. To achieve adequate blood cholesterol measurements and to minimize the effect of interfering substances, modifications in reagents

and/or instruments may be necessary.

Serum cholesterol can be measured using an enzymatic method based on cholesterol esterase and oxidase reaction as in the case of the DuPont ACA and the Reflotron instruments or by the more economic colorimeteric assay.[10]

Several studies have recently evaluated precision, accuracy, and bias associated with the use of the new portable desk top analyzers used for measurement of TBC.[76,77,80,81] It has been concluded that the use of these instruments, when operated according to the manufacturer's recommended procedures, demonstrated acceptable accuracy and precision that met those goals established by the NCEP. The characteristics of the three most commonly used instruments for large cholesterol screening programs are presented in Table III.[77]

In spite of the inconclusive establishment of the proper age at which screening for hyperlipidemia (HLP) should be initiated, most screening tests are done after puberty.[49] It has been recommended that individuals with a family history of hypercholesterolemia and those with xamthomas, pancreatitis, or very premature CHD in first degree relatives be screened before puberty. On the other hand, those individuals with documented CHD in first degree relatives, women on oral contraceptives, most American men, and those with established risk factors should be screened between the age of 20 to 25. Lastly, everyone 20 years and older should check his/her blood cholesterol level

Table III:

Accuracy Study:[1] Cholesterol Testing of Three Office Chemistry Instruments Compared With LRC[2] Results Using NCCLS[3] Guidelines for Method Comparisons.

Instrument	N	Mean[4] mg/dL	Slope	Y-Intercept mg/dL	r	SE[5] mg/dL	Total Bias %
Abbott Vision	83	223	1.06	1	0.98	12	+ 3.9
Boehringer Mannheim Reflotron	83	225	0.79	18	0.97	13	+ 4.5
Kodak Ektachem DT 80	83	211	0.9	20	0.98	10	- 1.8

[1]Adapted from Reference #77, p.3446.
[2]Lipid Research Clinic.
[3]National Committee for Clinical Laboratory Standards.
[4]LRC Mean equals 215 mg/dL.
[5]Standard Error.

every five years and more often if the patient is obese, smoker, hypertensive, or diabetic.[49]

Albeit the intensive effort of the NCEP to encourage the public to know their cholesterol level, only 29-57% of adults have had their cholesterol checked nationwide.[39] In fact the month of April 1988 was denoted as "National Know Your Cholesterol Month" in recognition of the need for federal, state, and local activities to support cholesterol awareness. Health care providers are encouraged to take the initial steps to inform their patients of their cholesterol value and what it means.[39]

Special attention should be paid to four subgroups in which it is wise to monitor and treat HLP, even with no significant elevation in serum cholesterol. The first category includes post coronary bypass patients where angina and new vein graft occlusion reoccur in a predictable number of them. The second category consists of patients on chronic renal dialysis, where atherosclerosis is often markedly accelerated. The third category represents patients with Tangier disease, a rare disease where HDL is almost totally absent. The fourth category includes patients with moderate or severe elevated triglyceride levels, particularly in those with hereditary deficiency of lipoprotein lipase (Type I & V phenotype).[49]

<u>What Lipoprotein Fraction Should Be Measured</u>?

For screening purposes, it has been recommended to measure total blood cholesterol (TBC) in a non-fasting

state. Many studies have shown that high levels of LDL and TBC are strong risk factors for atherosclerosis and CHD.[7,18] Although LDL is the actual target of cholesterol-lowering efforts, TBC can be used instead during the initial screening tests. The use of TBC as a screening tool is more available, less expensive, and does not require the patient to fast for 10-12 hours before the test. Furthermore, it has been demonstrated that both fasting and non-fasting measurements of TBC are equally reliable.[4,18,20,75,82,83] In addition, it has been reported that TBC is not altered by the cholesterol or triglyceride content of meals, and therefore, there is no reason to use any other measure of blood lipids initially.[7,18,20,75,82]

When screening individuals for elevated blood cholesterol, the objective is not simply to label or classify the patients but rather to take preventive measures early in the disease state. Advancing the time of diagnosis, through initial TBC screening and referral procedures, might have a desirable prognostic value. The effectiveness of such procedures can be enhanced if effective therapy could be started during the asymptomatic period.[84] Therefore, it is advocated that screening tests may have the potential to advance the time of diagnosis since survival is measured from the time of diagnosis rather than the time of onset. Mully[84] concludes that "...the survival of patients whose diseases are detectable by screening should be expected to be longer than that of

patients who present symptomatically." In addition, patients at risk of CHD who spend more time in the asymptomatic period, are more likely to be identified by screening tests than are patients with more aggressive disease, added Mully. It is important, however, to note that screening results should not be considered as definitive diagnostic tools.

Several considerations must be made before labeling patients with either high, normal, or low blood cholesterol. Diagnostic evaluations based on the lipoprotein pattern rather than TBC level was suggested to enhance sensitivity and specificity.[14] Labeling individuals may produce its own morbidity and negative effect on health perception. Furthermore, labeling can also have a negative outcome on employability and insurability.[84] Since the treatment of HLP, either by dietary means or drug therapy can be life-long, expensive and sometimes exposes the patient to potentially hazardous side effects, it has been recommended to accurately evaluate patients for underlying risks of developing CHD including assessment of life style and drug and/or disease state influence.

In a study involving 8449 subjects intended to evaluate the efficacy of screening for dyslipoproteinemia (both hyper- and hypolipoproteinemia), it was found that more than 80% of all the hyperlipidemic participants had hyperlipoproteinemias. It was concluded that such lipid

screening provided a lower proportion of false-positive than false-negative results. In addition, most participants (>98%) without hyperlipoproteinemia (true negative) were correctly identified.[14]

General Versus Selective Screening

Selective screening may not serve as a sufficient means of reducing the incidence of CHD. This may be true since a large proportion of individuals at risk would not be examined if assessment was restricted to a targeted population with preestablished selected screening criteria. In addition, testing the cholesterol level as part of any first attendance medical examination (case finding approach) has been recommended to be the usual approach.[20] The overall goal of both the general screening and case finding approach is to recognize people with high levels of risk factors who require treatment.[53] It has been emphasized that "... detection of increased risk implies a commitment to provide continuing preventive care."[53]

Treatment of Hyperlipidemia

In spite of the extensive clinical data and epidemiologic evidence linking elevated blood cholesterol levels to CHD, some doubt and controversy remains about the strength of the causal relationship between the two parameters.[2,4,6,16,85] The National Institutes of Health (NIH) and the National Heart, Lung, and Blood Institute (NHLBI) assembled a consensus conference on lowering blood cholesterol to prevent heart disease held from December 10-12, 1984.[2] This conference was initiated to investigate the link of increased CHD with increased blood cholesterol, and to resolve the questions related to when to treat high blood cholesterol, and what should be done to diagnose such levels. This consensus panel met after the results of the Coronary Primary Prevention Trial had shown that "lowering blood levels of cholesterol actually has reduced the risk of heart attacks". This panel represented experts in a variety of disciplines including; cardiology, epidemiology, biostatistics, and experts on diet and nutrition, preventive and primary care medicine. The expert panel's goal was to get a consensus position on important and crucial questions. Among the questions raised were the following:[2,20,85]

1. Is there a causal relationship between blood cholesterol level and CHD?
2. Will reduction of elevated blood cholesterol help prevent CHD?

3. How and when should dietary and drug therapy be started? And under what circumstances?
4. What are the goals of treatment?

After hearing a series of presentations and reviewing all clinical and epidemiological data, the 1984 panel concluded that:

a. Elevated blood cholesterol is a major cause of CHD.
b. Lowering high cholesterol level (especially LDL) would help, beyond any doubt, in reducing the risk of CHD.
c. Everyone with a blood cholesterol level above the 75th percentile (at or above 240mg/dL) is recommended to be treated.[2,85]
d. Dietary change under the guidance of a physician, dietitian, or other health professional is the primary treatment for high cholesterol. If response to diet is not adequate, appropriate drug therapy should be added.
e. Since blood cholesterol levels of most Americans are undesirably high, which in large part is due to a large dietary intake of saturated fat and cholesterol, all Americans two years and older were advised to reduce their total fatty intake from the current level of 40% to 30% of total calories. Further, it recommended reducing saturated fat to less than 10% and increase polyunsaturated fat by no more than 10% of total calories, and reducing dietary intake of cholesterol to 250-300 mg or less daily.
f. Special attention should be paid to identify and manage

other underlying risk factors such as hypertension, cigarette smoking, diabetes, and obesity. It is important to point out that the NIH consensus panel guidelines[2] used to classify patients with blood cholesterol levels at the 75th and 90th percentiles based on patient's specific age (See Table IV (A)).

To establish a detailed set of new guidelines that provides practical advice for dealing with the adult patient's cholesterol problem, the National Cholesterol Education Program (NCEP) asked a panel of experts in 1987 to develop new guidelines for detection and management of high blood cholesterol.[85] The panel, which included experts representing a variety of disciplines and a wide range of expertise, worked for over a year to establish a consensus position on additional questions. Cleeman reported a list of these questions that included "...how to go about detecting and evaluating high blood cholesterol, at which levels of cholesterol to initiate treatment, what the goals of treatment are, how to use dietary therapy, and how and when to use drug therapy in addition to diet."[85]

This major panel carried out its work through three subcommittees, namely, (1) the subcommittee on prevalence, detection, diagnosis and evaluation; (2) the subcommittee on dietary treatment; and (3) the subcommittee on drug therapy. The report of the expert panel on blood cholesterol in adults was first published in January 1988, representing a true and highly collective agreement

Table IV (A):

NIH[1] Guidelines on Total Blood Cholesterol[2] (1984).

Assigned Risk of Coronary Heart Disease For Cholesterol		
Age	Moderate Risk	High Risk
20-29	> 200 mg/dL	> 220 mg/dL
30-39	> 220 mg/dL	> 240 mg/dL
40 and over	> 240 mg/dL	> 260 mg/dL

[1]National Institutes of Health.
[2]Adapted from Reference #2, p.2083.

Table IV (B):

NCEP[1] Guidelines Based On Total Blood Cholesterol[2] (1987).

Desirable Blood Cholesterol	Borderline-High Blood Cholesterol	High Blood Cholesterol
< 200 mg/dL	200-239 mg/dL	240 mg/dL & Above

[1]National Cholesterol Educational Program.
[2]Adapted from Reference #20, p.37.

position.[85] The panel recommendation is applied to any person who is 20 years and older regardless of sex.[20,29,85] These guidelines include the following characteristics:

1. The cutoff point at which interventions should be initiated is a total blood cholesterol of 200 mg/dL or higher.
2. Total blood cholesterol is used for initial case finding (screening) and monitoring the progress of dietary therapy, while LDL is used thereafter to refine the assessment of CHD risks and for establishing the final diagnoses.
3. The individual's overall risk of CHD must incorporate additional risk factors other than TBC level which influence the choice of cut points and goals of cholesterol targeted levels.
4. Cut points and specific goals for drug therapy are established that protect from overuse of lipid lowering drugs to achieve a cholesterol level that could have been reached by diet alone.[19] The NCEP expert panel report includes additional information dealing with an educational effort directed to all health care professionals including physicians, pharmacists, and dieticians. Furthermore, an overview and summary of classification, prevalence, detection, and evaluation of elevated blood cholesterol, evidence and magnitude of the link between high cholesterol and CHD and a step-wise approach of dietary and therapeutic treatment

are also presented.[20]

For initial screening of blood cholesterol, a non fasting state is recommended by the expert panel. Individuals are to be classified into one of three classes based upon their cholesterol level {See Table IV (B)}. A cholesterol level below 200 mg/dL, regardless of age or sex, is considered "desirable or normal". Persons within this class are advised to repeat their cholesterol test within 5 years from the initial screening and be assessed for other CHD risk factors and be given dietary and risk reduction information. A borderline-high blood cholesterol is referred to as blood cholesterol level of 200-239 mg/dL that needs to be rechecked annually. Patients in this second category who do not have a history or evidence of heart disease and/or less than two risk factors should be advised to start a "step-1" diet. The goal of such dietary therapy is to minimize the consumption of saturated fat to less than 10%, cholesterol to less than 300 mg/dL, and increase the carbohydrate intake to 50-60% of total calories. Total blood cholesterol should be checked at 4-6 weeks and at three months after starting the step-1 diet to assess dietary intervention. If dietary goals have not been achieved, lipoprotein analysis should be initiated to determine LDL level. If the LDL level is found to be normal (less than 130 mg/dL), the patient should be advised to maintain a prudent diet and reduce controllable risk factors such as elevated blood pressure, cigarette smoking,

and high blood sugar. The patient is then advised to recheck his/her total blood cholesterol quarterly for the first year and twice yearly thereafter.[20,24] There are two options for people who have borderline-high blood cholesterol who failed the step-1 diet. He/she may be referred to a registered dietician to either retry this step-1 diet or start the step-2 diet (See Table V), based on clinical and risk factor considerations. Cholesterol is then remeasured in 3-6 weeks and at 3 months. Patients at high risk of developing CHD, TBC of more than 240 mg/dL or borderline-high risk plus definite heart disease and/or two additional risk factors, including male sex, should have a lipoprotein analysis done. In addition, a complete family history and clinical evaluation including screening for secondary causes (drug and/or disease induced) of hyperlipidemia (HLP).

If LDL level was found to be normal, TBC should be repeated every five years and dietary and risk reduction information should be provided. In contrast, if the patient was found to have a borderline-high LDL (130-159 mg/dL) with no heart disease or less than two CHD risk factors, a step-1 diet and the subsequent algorithm outlined above should be initiated and TBC should be evaluated annually. On the other hand, if the patient was found to have high risk LDL (160 mg/dL or higher) or has definite heart disease and/or two risk factors, a complete clinical evaluation should be started. Based upon the

Table V:

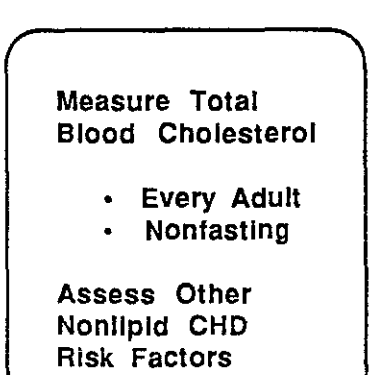
Dietary Therapy of High Blood Cholesterol Level.[1]

Nutrient	Recommended Dietary Intake	
	Step-One	Step-Two
Total Fat	< 30% of tc[2]	< 30% of tc
Saturated	< 10% of tc	< 7% of tc
Polyunsaturated	Up to 10% of tc	Up to 10% of tc
Monounsaturated	10-15% of tc	10-15% of tc
Cholesterol	300 mg/dL	< 200 mg/dL
Carbohydrate	50-60% of tc	50-60% of tc
Protein	10-20% of tc	10-20% of tc
Total Calories	to achieve and maintain desirable weight	

[1]Adapted from Reference #20, p.46.
[2]tc= Total calories.

patient's total blood cholesterol, LDL, coronary risk profile, clinical status, age and sex, initiating a selective hypolipidemic drug therapy should be considered.

For patients with borderline-high risk who have definite CHD or two risk factors as well as high risk groups, the goal of therapy is to lower LDL to below 130 mg and 160 mg/dL, respectively. The two dietary steps recommended by the panel in their report are very similar to dietary modifications recommended by the American Heart Association.[20] These diets are designed as part of a population-based program to progressively reduce the intake of saturated fats and cholesterol and to eliminate excess calories (See Table IV).[5,20] It has been emphasized that physicians should let their patients understand that the goal of dietary therapy is not a temporary diet, but rather a permanent change in their eating behavior.[20] A schematic approach of classification, evaluation, and step-wise treatment approach based on TBC and LDL levels is presented in Figures 2 and 3.[20]



Classification

<200 mg/dl	Desirable Blood Cholesterol
200-239 mg/dl	Borderline-High Blood Cholesterol
≥240 mg/dl	High Blood Cholesterol

Recommended Follow-up

Total Cholesterol <200 mg/dl	Repeat within 5 years
Total Cholesterol 200-239 mg/dl	
WITHOUTdefinite CHD or two other CHD risk factors (one of which can be male sex)	Dietary information and recheck annually
WITH definite CHD or two other CHD risk factors (one of which can be male sex)	Lipoprotein analysis; further action based on LDL-cholesterol level
Total Cholesterol ≥240 mg/dl	

Figure 2: Initial Classification and Recommended Followup Based on Total Cholesterol. (Adapted from Reference #20).

Do Lipoprotein Analysis:

- 12 hour fast
- Measure total cholesterol, HDL-cholesterol, and triglycerides
- Estimate LDL-cholesterol= total cholesterol – HDL-cholesterol – (triglycerides/5)
- Average of 2 to 3 measurements, 1 to 8 weeks apart

Classification

<130 mg/dl	Desirable LDL-Cholesterol
130-159 mg/dl	Borderline-High-Risk LDL-Cholesterol
≥160 mg/dl	High-Risk LDL-Cholesterol

Dietary Treatment

	Initiation Level	Minimal Goal
WITHOUT CHD or two other risk factors	≥160 mg/dl	<160 mg/dl
WITH CHD or two other risk factors	≥130 mg/dl	<130 mg/dl

Drug Treatment

	Initiation Level	Minimal Goal
WITHOUT CHD or two other risk factors	≥190 mg/dl	<160 mg/dl
WITH CHD or two other risk factors	≥160 mg/dl	<130 mg/dl

Figure 3: Classification and Treatment Decision Based on LDL-Cholesterol (Adapted from Reference #20).

Dietary Fish and Fibers

It has been observed epidemiologically that cardiovascular mortality in Greenland Eskimos and the Japanese is relatively lower than that of the Western industrialized world.[86,87] This difference is believed to be related to the protective effects of their diet which consists mainly of fish and marine foods in general. It is well known that most marine foods contain large quantities of omega-3-fatty acids, namely, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Several reports pointed out the beneficial effect of omega-3-fatty acid consumption on cardiovascular disease.[6,20,86,87] These reports demonstrated that these fatty acids can decrease triglycerides and cause a small decrease (or sometimes increase) in LDL cholesterol with no effect on HDL.[88] However, it has been reported that "No studies are available either comparing the effectiveness and safety of fish oil with other lipid-lowering drugs or showing that fish oil causes regression of atheromata or decreases the incidence of coronary heart disease."[88]

Several mechanisms have been proposed for the potential beneficial cardiovascular effects of fish oil. The following are the major mechanisms proposed:

1. Reducing the hepatic VLDL and fatty acid synthesis.
2. Increased VLDL elimination.
3. Enhanced fecal steroid excretion.
4. Interfering with platelet aggregation which plays a

key role in thrombosis and promotion of arterial smooth muscle cell proliferation.

5. Alteration of monocytes and neutrophil function, thereby prevent formation of fatty streaks and fibrous plaque formation.
6. Reduction in blood pressure in patients with mild hypertension.

It is important to keep in mind that fish oil consumption, especially in large amounts, may cause bleeding due to decreased platelet aggregation and increased bleeding time and, therefore, should be used with caution, if at all, in patients on anticoagulants or those with an active bleeding condition. This seems to be in accord with what has been reported in that Eskimos have a twofold higher incidence of stroke than citizens of Western countries.[29,87] In addition, ingestion of large amounts of certain fish oils may contain toxic amounts of vitamin A and D. Overall, however, fish in general is considered a useful substitute for meats (which are rich in saturated fats) and may be of value in lowering triglyceride and cholesterol levels with minimal harmful side effects.

Dietary ingestion of approximately 15-25 gram/day of soluble fibers was reported to be associated with a 5-15 mg/dL reduction in plasma cholesterol.[20] Oat products and beans, which contain a beta-glycan gum, pectin, and psyllium (e.g., Metamucil) were found to possess similar effects on blood lipids.[20,89,90]

In a double blind, placebo-controlled parallel study, the effect of Metamucil (which contains 79% psyllium hydrophilic mucilloid) was found to reduce total blood cholesterol (TBC) by 14.8%, LDL level by 20.2%, and the ratio of LDL/HDL by 14.8% compared to baseline values.[89] This effect was seen in response to 3.4 grams of psyllium three times per day for eight weeks, after a two-week baseline period. Impressively, psyllium treatment had no significant effect on body weight, blood pressure, HDL, triglycerides, or blood glucose.

Short term effects of psyllium supplements was reported to lower TBC by about 16%, while long term effects of dietary fibers from oat and bean reduced blood cholesterol by more than 20% and this effect was reported to last for at least 2 years in hypercholesterolemic men.[91] In the Fagerberg study,[90] Metamucil was reported to possess a safe and long acting effect on fasting blood glucose and serum cholesterol.

Although these clinical studies documented the hypoglycemic and hypolipidemic effects of soluble fibers (a 20-30% reduction in TBC), the American Heart Association diet (which lowers TBC by 3-7%) does not include dietary fiber as an approach to lowering blood cholesterol. On the other hand, some experts still question dietary fiber usefulness as a therapeutic modality.[91] However, it has been reported that patient compliance with dietary fiber treatment was excellent with no observed clinically

important side effects.

Drug treatment

It is to be emphasized that treatment of HLP by dietary means remains the cornerstone in the management of patients with elevated lipids. Dietary therapy should be tried for at least six months, or for 12 months if indicated by a physician, before considering drug treatment. This is because drug treatment can be tedious, lifelong, involves cost to patients, and poses potentially hazardous side effects. Therefore, consequences of anti- hyperlipidemic medication should be considered before starting drug therapy. Characteristics of drugs used to treat high blood lipid are presented in Table VI.[24] The bile acid sequestrants (cholestyramine and colestipol) and nicotinic acid are considered the drugs of first choice in the management of hyperlipidemia. These two drug categories lower the risk of CHD in clinical trials as well as have established long-term safety.[20] If used in the recommended dose, a 15-30% reduction in LDL level is expected. These two categories require considerable patient education in terms of how to take the drug and what to do to reduce the risk of side effects to improve patient compliance. It has been reported that bile acid sequestrants are often associated with increased triglyceride levels (equal or more than 250 mg/dL) due to increased hepatic VLDL synthesis. Therefore, in patients with concurrent hypertriglyceridemia and hypercholesterolemia, nicotinic

Table VI:

Characteristics of the Hypolipidemic Drugs.[1]

Agent (Brand Name)	Effect on lipoprotein	Reduced risk of CHD[2]	Long-term safety	Maintaining adherence	% Lowering LDL[3]	Daily dosage	Cost[4] ($)
Cholestyramine (Questran)	Dec[5] LDL	Yes	Yes	↑ Require considerable patient education	15-30	12-16g	57.60
Colestipol (Colestid)	Dec LDL	Yes	Yes		15-30	15-30 g	41.07
Nicotinic Acid (Nicolar)	Dec LDL, Inc[6] HDL[7] Dec VLDL[8]	Yes	Yes	↓	15-30	3-6 g	58.82
Lovastatin (Mevacor)	Dec LDL, Inc HDL	Not proven	Not established	↑	25-45	40-80 mg	46.88
Gemfibrozil (Lopid)	Dec LDL, Inc HDL	Yes	Yes	Relatively easy	5-15	1200 mg	41.63
Clofibrate (Atromide-S)	Dec VLDL, May Inc HDL	Not proven	Not established	↓	No effect on LDL	1-2 g	44.20
Prubucol (Lorelco)	Dec LDL, Dec HDL	Not proven	Not established	↓	10-15	1 g	45.50

[1]Adapted from References 16, 24, 35, and 88.
[2]Coronary Heart Disease.
[3]Low density lipoprotein.
[4]Cost to pharmacist for 30 days' treatment.
[5]Dec=Decrease.
[6]Inc=Increase.
[7]HDL=High density
[8]VLDL=Very low density lipoprotein.

acid is the drug of first choice.

The 3-hydroxy-3-methyl-glutaryl coenzyme-A reductase inhibitor (HMG-Co A), lovastatin, is a new member of a class of drugs that has been classified as a second line for treatment of lipid disorders. They are effective in lowering LDL (25-45% reduction), increasing HDL with an excellent level of compliance. Since this drug category is relatively new, its effectiveness in preventing or reversing atherosclerosis and CHD as well as its long-term safety have not yet been established.[20] However, lovastatin (in 20 mg and 40 mg twice daily) in a 12-week study in 264 patients has been shown to be more effective in lowering LDL and TBC and better tolerated than cholestyramine (12 grams twice daily).[92]

Gemfibrozil (Lopid) is a drug that belongs to the Fibric acid category which is effective in lowering plasma triglycerides and VLDL while increasing HDL. In a recent five year blind trial (the Helsinki Heart Study), Lopid has been shown to decrease triglyceride and LDL levels and increase HDL in 4,081 asymptomatic men.[83,93] This study has proven the effectiveness of the drug in decreasing the number of myocardial infarctions (56 in Lopid group vs. 84 in placebo group) and therefore, is associated with low incidence of CHD.

Probucol (Lorelco) and clofibrate (Atromid-S) are primarily effective for lowering triglyceride levels. However, probucol may decrease HDL in addition to its

significant side effects. Clofibrate may increase LDL, decrease libido, and increase gallstone and tumor formation. Therefore, these two drugs are not yet approved by the Food and Drug Administration for routine use in lowering elevated blood cholesterol levels and are considered to be last resort drugs.

Community-based Cholesterol Screening

A community-based cholesterol education program should give high priority to the goal of detection and intervention. However, in the past, several barriers to this goal have existed.[94] These barriers include the necessity for venipuncture by trained personnel to obtain blood samples, the expense of laboratory tests, the delay between sample collection and receiving the test results, and the lack of standardization for cholesterol determination across clinical laboratories. Fortunately, new guidelines were recommended in 1987 and new cholesterol values were clearly established. Furthermore, patient education material and affordable and accurate portable equipment became available to facilitate community-based cholesterol screening programs. Nevertheless, with these more restricted guidelines, a majority of individuals would be expected to experience difficulties with adherence to these guidelines or goals.[94]

Two pilot community-based cholesterol determination studies utilized the portable Kodak analyzer (EKTACHEM-DT60) where the blood sample was collected from a finger

puncture.[94,95] In the Lefebvre[94] cholesterol screening and education campaign, 1439 participants were recruited through extensive media coverage from March to April 1985. It was reported that nearly 60% of recruited individuals were found to have blood cholesterol levels that exceeded recommended goals (TBC < 200 mg/dL). A series of cholesterol Screening, Counseling and Referral Events (SCOREs) were conducted several times weekly during the two month campaign. Cholesterol screening events were conducted in 21 sites including several churches, shopping plazas, local businesses, local area drug and retail stores. Two months from the initial screening, three hundred ninety nine individuals (27.7%) individuals had not returned for the second cholesterol measurement. Nearly sixty percent (57.69%) of the remaining 1040 persons had successfully reduced their blood cholesterol by an average of 29.1 mg/dL. In contrast, 423 persons (40.67) had an increase in blood cholesterol and additional 17 persons (1.63%) had no changes.

The second study was conducted in the New York metropolitan area and lasted five days.[95] At the end of the study period, 12,432 participants had been tested at six sites including five hospitals and a health education facility. Approximately half the population reported that they had their cholesterol checked previously. Three hundred participants from the original screening were contacted by a telephone survey. Eighty eight claimed that

they saw their physicians (29.3%), however 57% of them reported that their physician did not measure their cholesterol again to confirm the initial screening results. Unfortunately, 54% of respondents received no advice from their physicians, while 36% reported that dietary changes were recommended. Surprisingly, 71% of individuals with cholesterol levels between 221-260 mg/dL were advised to do nothing and not to worry.[95] This indicates the need for cholesterol education programs which must be directed not only to the public but also to physicians. Referrals for lipoprotein analysis and initiation of dietary or lipid-lowering drug therapy would be a major problem if physicians are not taking the appropriate steps to bring their patients' blood cholesterol down to acceptable levels.[94]

Several studies demonstrated the possibility of implementing community screening programs that targeted toward motivating more people to become aware of their cholesterol levels.[96] Educational programs should be targeted toward providing those with high serum levels the necessary information to help lower their cholesterol. General dietary recommendation, food selection, and follow up protocols to assess patient response to dietary changes and lowered cholesterol level has been emphasized.

Scope Of The Study

It was pointed out that the availability of accurate and portable blood cholesterol measurement equipment, that utilizes blood obtained from a finger stick, facilitates screening efforts, especially for pharmacists.[32] Several advantages were reported to be associated with such health care program at community pharmacies. First, pharmacies have a wide geographic distribution and are easily accessible. Second, pharmacists can provide professional information and provide educational materials that enhances the screening effort. Third, they can establish referral and monitoring programs for those patients with hyperlipidemia and counsel patients on side effects of drugs, if prescribed. This enhances the pharmacist's long-term contribution in controlling high blood cholesterol and CHD morbidity.

It has been reported that total blood cholesterol screening in a community pharmacy may be an important new opportunity in pharmacy practice. Providing such screening service offers pharmacists a unique opportunity to expand their patient-oriented clinical services which may prove to be a financially feasible public health activity.[29,97-99] Pharmacists can improve the public's awareness and understanding of the importance of lowering blood cholesterol. It remains to be determined if screening with long-term follow up in a community pharmacy is, in fact, effective.

This current research project was initiated to investigate the feasibility and outcomes of conducting a cholesterol screening program in a community pharmacy. It was targeted toward identifying individuals with elevated blood cholesterol levels and helping them control their levels. Follow up procedures, pre- and post-test survey, CHD risk factors assessment, and medication screening were considered as an integral part of the study. This project was also intended to evaluate the impact of this new patient oriented community service in terms of TBC level lowering and behavior changes. Acceptability of the project to the participants and willingness to pay for the proposed service if it were to be available in their community pharmacy was also evaluated. Long term follow up and referral service following the initial screening was investigated to determine its effectiveness.

GOALS AND OBJECTIVES

Goals:

1. To develop a model for screening, detecting, and referring ambulatory patients with elevated blood cholesterol in a community pharmacy.
2. To increase the patients' awareness and understanding of the value of lowering their blood cholesterol and its impact on the morbidity and mortality of coronary heart disease (CHD).
3. To establish a follow up procedure for those patients at high risk of developing CHD.
4. To identify patients with multiple risk factors and to encourage them to see their primary health care provider to establish the final diagnosis and adherence to treatment regimen, if indicated.
5. To provide motivation for patients with high blood cholesterol to lower their levels below 200 mg/dL.
6. To assess patients' acceptance of the model, its convenience, and potential utilization of screening procedures in a community pharmacy.

Objectives:

1. To investigate the role of a community pharmacist in screening and follow up of ambulatory patients for hypercholesterolemia in a community pharmacy.

2. To define criteria for the selection of the patient population accepted in this study.

3. To identify those patients with elevated blood cholesterol who require further evaluation, monitoring and/or treatment.

4. To provide appropriate educational material for all participants screened and answers to their questions about cholesterol and other related issues particularly those at high risk of developing CHD.

4. To determine the impact of this project on:

   a. The patients' awareness of the problem.

   b. Lowering blood cholesterol during the follow up period.

   c. The degree of participants' acceptance of the idea of screening cholesterol level in a community pharmacy.

   d. Participants' attitude in terms of convenience and future utilization of such service if it were to be available in their community pharmacies.

METHODOLOGY

General Description

This community pharmacy screening project was designed in an attempt to identify individuals with elevated blood cholesterol. Patients classified at moderate or high risk for developing CHD would be referred to their physicians for further evaluation and treatment.

At the time of the initial screening, a brief personal and family history was collected to assess those patients with potential risk factors for developing CHD. These collected data were used to identify those patients who were in need of referral and monitoring services.

Follow up blood cholesterol testing during the five month period allowed assessment of patients' serum cholesterol status and response to dietary and exercise changes. It also allowed the pharmacist to screen patients for potential drugs that could induce or exacerbate hyperlipidemia. Follow up visits served as an appropriate time to provide additional teaching and counseling. Test results at the initial screening without subsequent follow up testing might needlessly worry patients. Motivating those patients with multiple risk factors to see their physicians was emphasized as the determining step in controlling their high cholesterol level.

The study protocol and the consent form (See Appendix A) were approved by the University Joint Council on Human

Research. The project's screening procedures, patient interviews, referral service, and follow up testing were conducted in the Campus Pharmacy, University of the Pacific, Stockton, California.

Identification of Patients

a. Subject Recruitment

Two hundred and forty-one persons, including University of the Pacific students, faculty, and employees were screened for high blood cholesterol (200 mg/dL or more). Subjects were recruited through two advertisements in the University newspaper (The Pacifican) and signs posted around the campus.

For screening purposes, total blood cholesterol (TBC) was measured in a non-fasting state.

b. Inclusion Criteria

Patients were admitted to the study if they met the following inclusion criteria:

1. Participants must be between 18 and 60 years of age.
2. Participants must not know their cholesterol level and have not been told by a physician that they have high cholesterol level.
3. Patients must not be receiving cholesterol reducing agents.
4. Participants must not be dieting or exercising already to reduce cholesterol levels.
5. Participants must be available for follow-up

during the six month period of the study.

6. Participants must be ambulatory.

7. If female, participants must not be pregnant.

8. Participants must not be involved in other concurrent studies.

All participants with an initial TBC of < 200 mg/dL, the "Normal Group" were excluded from subsequent blood testing and were given educational materials on maintaining good eating habits and exercise level. They were advised to check their TBC within the next five years and to keep a record of their test results. Since blood sampling is an invasive procedure, a written informed consent form was provided to each participant. Two consent forms were used, the first was required by the University Committee on Human Research and the second was a release of liability requested by Boehringer Mannheim Diagnostics. After explaining the scope of the project, procedures involved, and accompanying hazards that might occur, each participant was asked to read the provided consent form and sign it. A carbon copy was given to each participant with the TBC test result at the initial visit. All participants were advised that the initial TBC test as well as the two subsequent follow up tests, when applicable, were free of charge. No fees were paid for any individual to participate in this study. In addition, participants were advised that the University of the Pacific has no special program by which it provides compensation for medical treatment if injury

occurs during biomedical or behavioral research.

c. Patient Population

One hundred sixty-four patients were found to have a normal TBC, i.e., less than 200 mg/dL at the initial screening (Visit #1). This group will be referred to as the "Normal Population". Out of the remaining 77 participants, 20 persons did not meet the inclusion criteria and therefore were excluded from subsequent testing and follow up procedures. This second group will be referred to as the "Excluded Group". The remaining patients (N=57) were included in this study. One month after the initial cholesterol testing (Visit #2), six of the included patients were unavailable for the follow up testing. Those patients were considered drop outs. All the participants on visit #2 successfully completed the second follow up testing (Visit #3) and, therefore, the total number in the "Drop Out Group" was six patients. The remaining 51 patients who completed the study from day one to the end of the study period will be referred as the "Study Group".

Data Collection

The following data were collected for the 241 participants during the initial screening:

1. Individual's name, sex, date of birth, weight, height, and telephone number.
2. Name of participant's family physician.
3. Smoking status and number of cigarettes consumed

per day.

4. Oral contraceptive use (females only).

5. High blood sugar.

6. Blood pressure.

7. Exercise level.

8. Family history of heart problems. e.g., Hypertension, angina, or heart attack.

9. Abnormal thyroid function.

10. Educational level.

11. Low fat/weight control diet.

12. Name and number of medications used on a chronic basis.

13. Total number of risk factors (see list on page 73).

14. Initial total blood cholesterol level.

In addition, the following data were collected for the 51 participants who completed the study (the study group):

1. Initial TBC level and the subsequent two follow up levels.

2. Pre-test and post-test survey scores.

3. Patient's dietary and/or behavior modification in visit #2 and #3 as a result of knowing his/her initial TBC level.

4. Patient's attitude toward the idea of blood screening tests in community pharmacies.

5. Convenience and future utilization of such service if it were to be available in their neighborhood pharmacy.

6. Indication of patients' willingness to pay for this service and proposed fees.

7. Number of patients who had seen their physicians to establish the final diagnosis.

8. Number of patients who actually received a physician's order for lipid analysis as a result of the pharmacist's referral service.

Participants were assured that any information that was obtained in connection with this study that could be identified with them would remain confidential and would be disclosed only with their permission.

Selection of Instrument

The Boehringer-Mannheim analyzer (REFLOTRON) was used to determine cholesterol levels of the participants in this study. All auxiliary instruments, devices, and supplies were provided through Boehringer Mannheim Company.[a] The Reflotron analyzer was chosen because of the following features:

1. It utilizes dry chemistry reagent tabs (no need for blood dilution or centrifugation).

2. It requires only 30 uL (about 2 drops) of whole blood that can be obtained from a finger stick.

3. It gives relatively accurate and reproducible results (< 5% bias) in less than three minutes.

4. It requires minimal training and operating

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[a]Boehringer Mannheim Diagnostics. 9115 Hague Road. Indianapolis, IN 46250

skills.

5. It can detect blood cholesterol levels in the 100-406 mg/dL range.

Reflotron Operation Procedures

Operating the Reflotron analyzer is simple and involves the following three steps based on the manufacturer's recommendation:

1. Turn on the power switch and wait for the analyzer to warm up, the word 'READY' will be displayed. Insert a cholesterol calibration tab, which carries a programmed magnetic code, into the Reflotron and close flap. In a moment, a 'CHOLESTEROL PROGRAM' message is displayed on the LED screen. Open flap and remove the programmed tab in its original vial for next day use. This calibration procedure can be avoided by the use of individually programmed reagent tab which is slightly more expensive than the uncoded tabs.

2. Remove reagent tab (the uncoded tabs were used in this study for economic purposes) from vial and close vial. Remove the protective foil. Carefully draw blood sample into capillary tube, avoiding air bubbles. Dispense blood sample (30 uL) onto center of red mesh area of tab using a quick, smooth motion. Do not allow pipette tip or capillary tube to touch the tab.

3. Immediately insert tab with the reagent pad side up, until a click can be heard. When 'CLOSE DOOR' appears on the display, close the door.

Test name abbreviation 'CHOL' and countdown from 175 seconds to one will appear on the display. When time is up, test result will be displayed automatically, expressed in mg/dL. Open door, remove tab. All materials that came in contact with blood, such as capillary tubes and lancets, were discarded in a biohazard container.

Quality Control

A. CHECK TABS: (Checking the optical system)

Each week, a check test is performed to check the performance of the optical system of the Reflotron. The manufacturer's recommended test procedures are as follows:

1. Switch on the Reflotron. Take a new check strip out of vial and close vial immediately.

2. With no blood sample applied, insert the check strip into the instrument and close flap.

3. The display 'CHECK' confirms that the coded data have been correctly read into the instrument. In about two minutes, a set of three-digit values shows on the display.

4. Compare each of the three values with the corresponding reference value (mean) displayed on the vial label. If the three values displayed are within the specified confidence limits, the optical system is functioning properly.

B. CONTROL SERA: (Checking the entire system)

A universal sera (Precinorm U, Boehringer Mannheim Diagnostics) is used for checking the entire system. It consist of a freeze-dried control that is reconstituted by

dissolving the content of the vial in exactly two milliliters of redistilled water. Gently swirl vial for 30 minutes, do not shake vial to avoid the formation of foam.

1. Apply a control sera to a reagent tab using the Reflotron Eppendorf pipette, which uses disposable tips and insert the tab into the instrument.

2. Compare the values displayed to control sera range printed on the package insert (usually 163-221 mg/dL). If test value falls outside range, repeat test.

Control sera should be stored at 4°C after being reconstituted. A new vial is recommended to be used every week.

Initial Blood Cholesterol Screening

During the initial total blood cholesterol (TBC) test (Visit 1), each participant was asked to read and sign two consent forms (Appendix A) before obtaining the blood sample. An alcohol swab was used to clean the participant's finger and excess alcohol was gently wiped out using a 2X2 inch sterile pad. Surgical gloves were used during blood manipulation procedures to avoid direct blood contact. A finger stick was performed using an AUTOCLIX™ (Boehringer Mannheim Diagnostics) device that utilizes a sterile lancet. The first drop of the participant's blood was discarded to ensure an uncontaminated sample. Thirty microliters of blood were collected in a small capillary tube which is internally coated with heparin lithium to guard against blood

coagulation. The drawn blood sample was then analyzed using the standard testing procedures mentioned previously. Within three minutes, participant's TBC result in mg/dL was displayed on the screen.

During the three minute waiting period each participant was asked to fill out a cholesterol data sheet (Appendix B) which include personal data and a health questionnaire intended to assess the patient's underlying CHD risk factors. Participants' exercise level was determined based on a 4-point scale ranging from zero (non-active) to three (active). Educational background or the number of years spent in learning was classified into five categories. Participants with the highest educational level (Postgraduate degree such as M.S. and Ph.D) were given a value of 5, whereas participants with the minimal degree of education (Grade School) were give a value of 1 (Appendix B).

Assessment of Risk Factors

In order to assess the number of CHD risk factors the person might have, the following list of established risk factors was used in this project:[a]

1. Male Sex.
2. Hypertension.
3. Diabetes Mellitus.
4. Use of oral contraceptives.

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[a]CHD risk factors selected from References 12, 13, and 37.

5. Severe obesity (> 30% overweight).
6. Hypercholesterolemia (TBC > 200mg/dL).
7. Family or personal history of heart attack
8. Sedentary lifestyle (Physical inactivity).
9. Cigarette smoking (10 or more cigarettes per day)
10. Definite coronary heart disease, e.g., M.I.

Subclassification of Screened Population

Subjects with an initial TBC of < 200 mg/dL were assured that they had a normal level and were given instructions to check their TBC in the next five years. They were also advised to follow a good and balanced diet and to maintain an ongoing exercise program. All participants were asked to fill out a pre-test survey which assessed their knowledge and understanding of high blood cholesterol and the consequences of untreated high levels (Appendix C). Each participant went home with a nutrition handout and brochures which provided up to date information about maintaining a normal cholesterol level and good dietary intake (Appendix D). A specially designed cholesterol screening wallet card was given to all participants with their TBC result recorded and dated (Appendix E).

Subjects with an initial TBC of 200 mg/dL or higher, who fulfilled the project's inclusion criteria, were invited to participate in the study. They were informed that two follow up TBC tests during the next five months

would be requested. To be eligible for such follow up testing, patients were asked to sign a preliminary evaluation sheet (Appendix F). This signed evaluation sheet provided the authority for the project investigator to perform additional TBC testing, to refer patients to their family physicians or suitable health care center. In addition, it gave the investigator the legality to receive a copy of lipid analysis results performed at a standard laboratory for follow up purposes.

Follow up Testing and Procedures

Between the period of the initial screening and the first follow up test, patients with high TBC and additional risk factors were contacted by phone. This was intended to motivate them to see their physician for further evaluation.

On the first follow up test (Visit 2), TBC was checked using the same testing procedures mentioned earlier. Test results were recorded in the patient's wallet card and any TBC difference from the first visit was calculated for each patient. Patients who demonstrated a decline in cholesterol level and those who did exercise and modified their dietary intake of fats and cholesterol were encouraged to continue doing so. However, patients for whom there was no improvement or slight increase in TBC were advised to take a more active role in controlling their TBC and to seek dietary council and medical intervention. Possible dietary changes and the value of

initiating exercise program was again reinforced. This visit was an excellent opportunity to answer patients' questions concerning risk factors, dietary changes, TBC, and coronary heart diseases.

At the time of the second follow up test (Visit 3), 51 patients had their TBC tested. They were provided with a list of eight blood tests available and were asked to circle the number of test(s) they would use in the future if these tests were to be available in their community pharmacy (Appendix G). They were also asked to answer a post-test survey that includes five repeated pre-test questions to assess any change in attitude and knowledge of cholesterol and its association with heart disease (Appendix H), and to express their personal opinion and attitude toward the idea of blood screening in community pharmacies. Finally, a certificate of participation was awarded to all patients who completed the six month study in recognition of their efforts to lower their TBC and to reduce their chance of having coronary heart problems (Appendix I).

Statistical Analysis[a]

Several methods of statistical analysis, both parametric and non-parametric, were used to detect the significance of differences among means of the tested parameters. All statistical methods in this study were applied at a probability level of less than 0.05.

In order to compare results of certain parameters, the values obtained were coded first. The study group participants whose age was between 18-34 years of age were coded a value of one, whereas those 34-60 years old were coded a value of two. Similarly, total blood cholesterol (TBC) values were assigned a coded value of one (TBC of 100-199 mg/dL) and to a value of two (TBC of 200-400 mg/dL). The following is a list of the statistical analysis methods used in this project:

1. A one-way analysis of variance was used to determine the difference between the means of TBC levels in visit #1, #2, and #3 and used again to determine whether there was a significant difference between the four educational background levels.

2. Scheffe's Post Hoc Test was used to compare differences between the mean TBC levels for statistically significant F-Test results.

3. Student t-test was used to determine whether there

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[a] All statistical analyses were performed on the Fortune 32:16 computer, using the Minitab statistical program. Fortune System Corporation, Belmont, California. 1982.

was a significant difference between two groups when applicable, while two sample t-test was used to compare the difference between two sets of data containing unequal patient numbers, e.g., the study group (N=51) versus the normal group (N=164).

4. Two sample t-test was used to analyze coded data such as age, education background, sex, exercise levels, and difference in TBC results using the Reflotron analyzer against those obtained via standard laboratories.

5. The non-parametric Mann-Whitney test was used as an alternative for the t-test for the difference between two independent samples (number of risk factors in the study group versus those of the normal population) assuming samples were drawn from an unequally distributed population.

6. The correlation coefficient (r) was calculated for 13 different parameters to estimate the level of correlation between examined parameters.

7. Chi-square analysis was performed to compare sex distribution between the study group against the normal group.

Total blood cholesterol results of the three visits along with pre-test, post-test results, and patients' demographic data are presented in the results section.

RESULTS AND DISCUSSION

The relationship between elevated blood cholesterol and increased risk of coronary heart disease (CHD) has been well documented during the past 10 years. There is now solid evidence demonstrating that a 1% decline in serum cholesterol results in a 2% reduction in risk of CHD.[4,2,5,32] The National Cholesterol Educational Program (NCEP) was initiated in November 1985 to contribute to lowering morbidity and mortality from CHD by lowering cholesterol in those who are at risk. The NCEP program's main goal was to motivate all adult Americans to know their cholesterol level by attending cholesterol screening programs and to ask their physicians to have their cholesterol tested. However, less than half the adult population (29-57%, Median 47%) have had their cholesterol tested, according to the 1987 Behavior Risk Factor Surveillance System from 33 states.[90] In addition, only 6% of adults surveyed were able to provide a value for their cholesterol level (range 1-19%). This was attributed at least in part to the problem of accessibility to and/or the high cost for cholesterol test.

Now, with the availability of whole blood dry chemistry analyzers, a non-expensive total blood cholesterol (TBC) test can be performed in less than five minutes in a non-fasting state. Although the goal of dietary or drug treatment is to lower LDL level, patients can be monitored

on the basis of their TBC which serves as an indirect test of LDL. Measuring TBC has the advantage of low cost, the use of non-fasting blood specimens involved in the measurement, and the minimal amount of blood (two drops) required. A strong demand for establishing cholesterol screening programs was addressed as an effort to encourage more people to know their cholesterol level and what it means.

This research project was conducted to investigate a cholesterol screening and referral service in a community pharmacy. It was theorized that an easily accessible community pharmacist could identify those patients at risk of CHD through blood cholesterol measurement and from both personal and family data. This research project, in contrast to any other published study, was also designed to evaluate the impact of such proposed service on patient outcomes in terms of blood cholesterol lowering during a six month period, changes in behavior, referral to physician and patient acceptance of the service. The project was not intended to evaluate its impact on morbidity or mortality because of the limited study period. The project's flow chart and time line is depicted in Figure 4.

During the initial screening period (Visit #1), a total of 241 participants were screened for elevated total blood cholesterol (TBC) in a non-fasting state. It is important to point out that the number of persons tested per day may

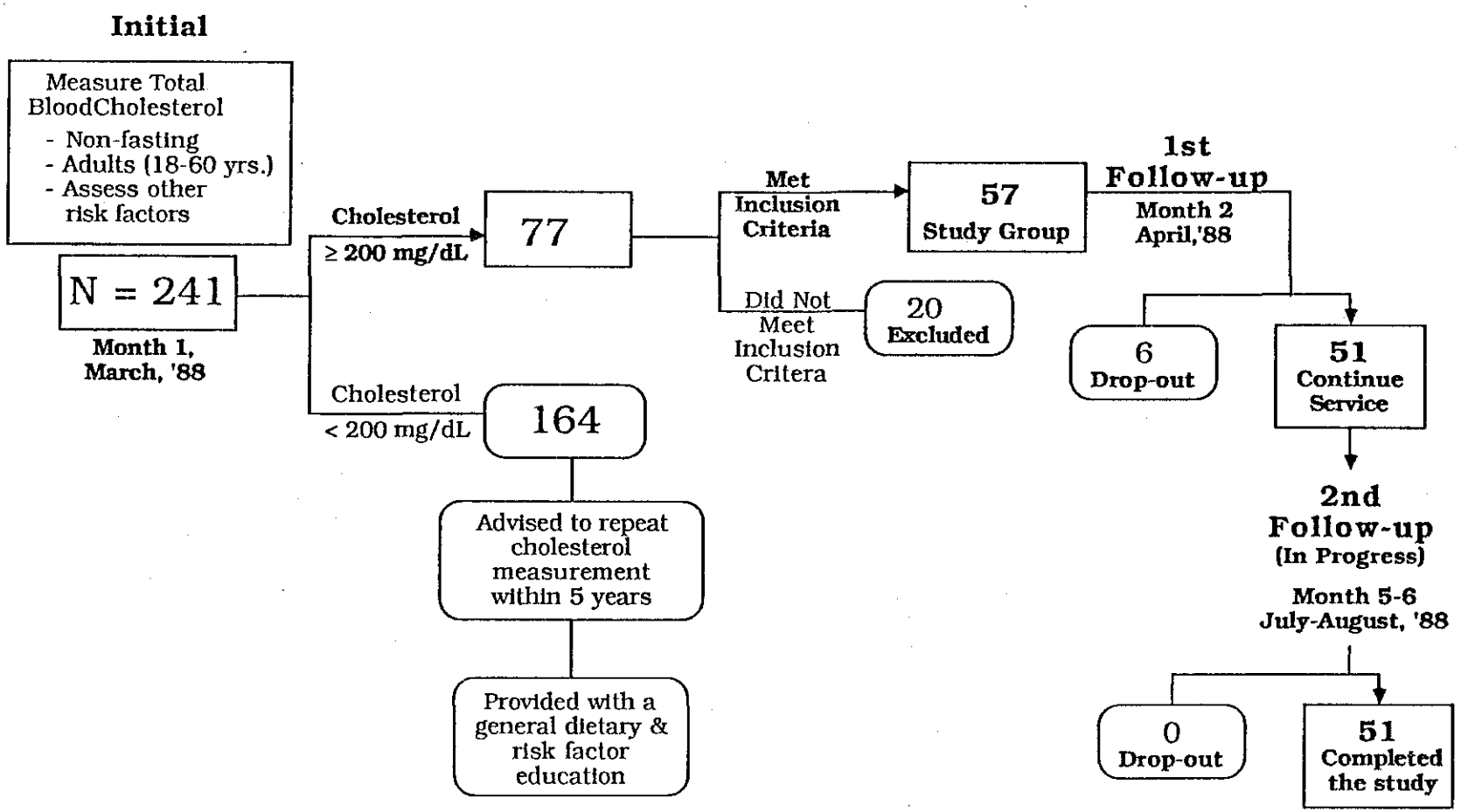


Figure 4: Flow Chart and Time Line of the Cholesterol Project

vary considerably between studies depending on several factors. These may include the number of screening sites involved in each screening program, the nature and the goal of such program, proposed or required fees for providing such service, method of follow up if any, and the length of the research study or screening program.

Ninety three participants out of the initial 241 stated that they had their blood cholesterol checked (38.58%), which is less than but close to the 1987 estimate of 47% (29-57%).

During the initial screening, one hundred sixty four participants were found to have a desirable blood cholesterol level (< 200 mg/dL) regardless of their age or sex. Selected demographic and statistical data for this "Normal Group" are presented in Table VII. All participants in this group were provided with general dietary and risk factor educational material (Appendix D). They were also advised to repeat their cholesterol measurement within the next five years and to record their levels in the cholesterol progress wallet card provided (Appendix E).

In contrast, 77 participants (31.95%) were found to have TBC > 200 mg/dL who had not been told previously that they had elevated cholesterol. This might have been due to the fact that their levels were considered to be normal based upon the 1984 guidelines. Surprisingly, 39 persons (50.65%) out of these 77 person with moderate to high

Table VII:

Selected Characteristics of Normal Population (Total Blood Cholesterol < 200 mg/dL).

Parameter	Value
Total Number Screened	164
Average TBC[1] (Range)	163.8 (100-199)
Average Age (Range)	29.97 (19-63)
Sex (Males:Females)	84:80
Family History of Heart Problems (%)	83 (53.66 %)
Family History of Heart Attack (%)	44 (26.83 %)
Average Number of Risk Factors (Range)	1.35 (0-3)

[1]TBC= Total blood cholesterol.

cholesterol levels had not had their cholesterol checked (against a reported 25.57% that was estimated from pooled results from 13,000 subjects).[96] In another five day screening study involving over 12,432 persons, it was reported that approximately 50% of these people never had their cholesterol level tested although 28% of them were found to be at moderate to high risk for CHD.[77]

According to the pre-established inclusion criteria, 57 participants out of the 77 persons with TBC of 200 mg/dL or over were accepted in the study (74.03%). The remaining 20 participants (25.97%) were excluded from further blood cholesterol testing and follow up procedures. Selected characteristics of these excluded persons are presented in Table VIII. One participant was excluded because she was pregnant (first trimester). It has been reported that pregnancy could lead to false lipid results due to hormonal and body fluid changes and she was advised that lipid analysis be performed six to nine months after delivery. Another two persons were 61 years old who had their TBC checked before and were told that they had high levels, therefore, were excluded. The remaining 17 excluded persons had their cholesterol checked previously and were told that it was high, including one who stated that his father, who is a practicing physician, would treat him.

The follow up procedure of this community pharmacy screening project consisted of telephone contact within 2-4 weeks of Visit #1 (the initial screening) and written

Table VIII:
Selected Characteristics of Excluded Patients.

#	Code	Age	Sex	# RF[1]	TBC[2]	FHx HP[3]	FHx HA[4]	Ed Bg[5]	Reasons for Exclusion
01	RG	36	MALE	4	203	YES	YES	4	CHK/TH[6]
02	CS	44	FEMALE	2	204	YES	NO	2	CHK/TH
03	BT	27	MALE	3	202	YES	YES	4	CHK/TH
04	CT	29	FEMALE	1	200	NO	NO	4	PREGNANT
05	IG	61	FEMALE	2	224	YES	NO	3	CHK/AGE
06	MD	24	MALE	3	245	YES	NO	3	CHK/TH
07	KC	51	MALE	5	300	YES	NO	4	CHK/TH
08	GN	57	FEMALE	3	234	YES	NO	3	CHK/TH
09	JE	58	FEMALE	2	255	YES	YES	3	CHK/TH
10	MC	58	MALE	3	204	NO	NO	5	CHK/TH
11	SC	55	FEMALE	3	217	YES	YES	2	CHK/TH
12	GD	46	MALE	3	288	YES	YES	5	CHK/TH
13	CF	61	MALE	4	217	YES	NO	2	CHK/AGE
14	SF	35	MALE	3	233	NO	NO	4	CHK/TH
15	CC	59	MALE	3	239	YES	YES	5	CHK/TH
16	RK	43	MALE	3	270	YES	NO	5	CHK/TH
17	DS	46	MALE	3	267	YES	YES	5	CHK/TH
18	HN	46	FEMALE	2	256	YES	NO	1	CHK/TH
19	MI	55	FEMALE	2	234	YES	NO	5	CHK/TH
20	RM	29	FEMALE	3	233	YES	NO	4	CHK/TH

[1]Number of risk factors.
[2]Total blood cholesterol.
[3]Family history of heart problems.
[4]Family history of heart attack.
[5]Educational background.
[6]Checked before and told high.

communication between Visit #1 (first follow up) and Visit #3 (the end of study period). The purpose of such communication was to remind the participant to adhere to a healthy diet and to maintain their regular exercise level, especially those with high TBC level and/or those at high risk of CHD. One month after the initial screening (Visit #2 or the first follow up test), six patients (10.53%) out of the 57 accepted participants were unable to attend this first follow up test and thus were placed in the "Drop Out Group". Table IX gives selected characteristics of this group. With the exception of one patient, all drop out patients left the state and therefore were unavailable for follow up (83.33%). Patient #5 showed no interest in the follow up testing and stated that she would see her physician to have a lipid analysis performed.

The remaining 51 patients, The Study Group, successfully continued the second follow up test (Visit #3) with no drop outs in spite of the two month gap between the two visits #2 and #3. This was thought as an initial indicator of the study group's interest and conscientiousness in knowing what might be the effect of dietary and/or behavior changes on their blood cholesterol levels. It is worth analyzing, at this point, the behavior of the study group in terms of their attending the second follow up with no drop out. It is possible to assume that these participants became more concerned and aware about their high cholesterol levels and therefore were willing to

Table IX:

Selected Characteristics of Drop-Out Patients.

#	Code	Age	Sex	# RF[1]	TBC[2]	FHx HP[3]	FHx HA[4]	Ed Bg[5]	Reasons for drop out
01	MM	19	Male	2	254	NO	NO	3	NAFF[6]
02	CC	24	Female	2	286	Yes	Yes	3	NAFF
03	SG	22	Male	3	209	Yes	Yes	3	NAFF
04	RM	45	Female	4	216	Yes	NO	4	NAFF
05	BP	35	Female	3	212	Yes	Yes	3	No interest
06	AN	34	Male	3	203	Yes	No	4	NAFF

[1]Number of risk factors.
[2]Total blood cholesterol.
[3]Family history of heart problems.
[4]Family history of heart attack.
[5]Educational background.
[6]Not available for follow up visits.

have more tests, in spite of the possible physical discomfort or inconvenience. It might also be a subjective measure of satisfaction with the project, because they could have chosen to not appear for the second test with no obligation. The comprehensive demographic and statistical data of the study group (51 patients) including their TBC on the three visits, personal and risk factors assessment data are presented in Tables X and XI.

Table XII summarizes major descriptive statistical data for the Study Group (N=51), the Normal Group (N=164), and the Total Population Group (N=241). Since the study group patients were included in the overall total population, all performed statistical analysis were based upon the difference between this group and the normal population group only, unless otherwise indicated.

General Comparative Analyses

The mean total blood cholesterol of the normal group was found to be 163.80 mg/dL which, because of the inclusion criteria, is significantly lower than that of the study group at 225.69 mg/dL ($P < 0.001$). A histogram presenting the TBC distribution of the three groups is presented in Figure 5. As can be seen, the TBC distribution of the total population exhibits a bell-shaped curve which is a characteristic feature observed in most clinical and epidemiological studies including the Framingham study. The study group represents the right half of the curve with TBC of 200 mg/dL and above, while

Table X:
Study Group Comprehensive Data.

TBC1[a]	TBC2[b]	TBC3[c]	% Change[d]	% Change[e]	Age	Sex[f]
230	175	182	23.9130	20.8696	21	1
235	237	224	-0.8511	4.6809	45	1
222	235	211	-5.8559	4.9550	39	1
289	285	273	1.3841	5.5363	40	0
228	217	216	4.8246	5.2632	27	1
210	193	195	8.0952	7.1429	22	0
219	227	237	-3.6530	-8.2192	52	0
221	229	181	-3.6199	18.0995	28	1
216	177	181	18.0556	16.2037	20	0
252	227	219	9.9206	13.0952	44	1
210	199	210	5.2381	0.0000	52	0
235	196	189	16.5957	19.5745	22	1
202	202	211	0.0000	-4.4554	60	0
251	221	266	11.9522	-5.9761	48	1
246	191	199	22.3577	19.1057	38	1
208	213	247	-2.4038	-18.7500	46	1
207	172	206	16.9082	0.4831	23	0
223	232	215	-4.0359	3.5874	24	0
204	203	204	0.4902	0.0000	60	1
223	197	208	11.6592	6.7265	27	0
216	209	164	3.2407	24.0741	26	0
231	168	180	27.2727	22.0779	24	1
200	176	234	12.0000	-17.0000	23	0
241	231	214	4.1494	11.2033	22	0
238	171	240	28.1513	-0.8403	22	0
210	169	157	19.5238	25.2381	22	0
256	198	194	22.6563	24.2188	24	0
242	190	229	21.4876	5.3719	28	0
206	197	199	4.3689	3.3981	27	1
214	196	185	8.4112	13.5514	46	0
217	201	192	7.3733	11.5207	58	0
204	217	204	-6.3725	0.0000	22	1
225	196	225	12.8889	0.0000	28	0
227	236	230	-3.9648	-1.3216	54	0
222	211	146	4.9550	34.2342	29	1
229	216	243	5.6769	-6.1135	52	0
257	227	236	11.6732	8.1712	60	0
214	229	216	-7.0093	-0.9346	21	0
214	203	157	5.1402	26.6355	23	1
284	236	281	16.9014	1.0563	56	0
201	179	199	10.9453	0.9950	29	1
213	184	184	13.6150	13.6150	46	1
201	198	180	1.4925	10.4478	48	0
239	225	220	5.8577	7.9498	45	1
209	193	179	7.6555	14.3541	40	1
215	215	215	0.0000	0.0000	43	0
300	235	225	21.6667	25.0000	31	1
208	174	191	16.3462	8.1731	52	1
212	197	201	7.0755	5.1887	45	0
202	173	195	14.3564	3.4653	53	0
232	157	178	32.3276	23.2759	21	0

[a]Total blood cholesterol, Initial screening (Visit # 1)
[b]Total blood cholesterol, Visit # 2
[c]Total blood cholesterol, Visit # 3
[d]% Change = (a - b) X 100
[e]% Change = (a - c) X 100
[f]1 = Male ; 0 = Female

Table X:
Study Group Comprehensive Data. (Continued)

Ed-Bg[a]	Ex-Lv[b]	# RF[c]	Pre-t[d]	Post-t[e]	V1-V2[f]	V1-V3[g]	V2-V3[h]
3	2	3	10	10	55	48	-7
5	0	5	10	10	-2	11	13
4	1	3	10	10	-13	11	24
3	0	5	10	10	4	16	12
4	1	3	10	10	11	12	1
3	0	2	10	10	17	15	-2
3	1	3	10	10	-8	-18	-10
3	1	3	10	10	-8	40	48
3	1	2	10	10	39	35	-4
5	1	2	10	10	25	33	8
2	1	1	8	10	11	0	-11
3	3	2	10	10	39	46	7
4	2	1	8	10	0	-9	-9
5	2	6	10	10	30	-15	-45
2	0	4	10	10	55	47	-8
5	3	3	10	10	-5	-39	-34
4	3	3	10	10	35	1	-34
3	1	4	8	10	-9	8	17
5	3	2	10	10	1	0	-1
4	2	3	10	10	26	15	-11
4	3	2	10	10	7	52	45
3	1	3	10	10	63	51	-12
4	2	1	10	10	24	-34	-58
3	1	2	10	10	10	27	17
3	2	2	10	10	57	-2	-69
3	2	1	10	10	41	53	12
3	1	3	10	10	58	62	4
2	3	4	10	10	52	13	-39
3	1	2	10	10	9	7	-2
3	2	2	10	10	18	29	11
5	1	2	10	10	16	25	9
3	3	3	10	10	-13	0	13
3	1	3	10	10	29	0	-29
4	2	3	10	10	-9	-3	6
4	2	3	10	10	11	76	65
3	1	1	10	10	13	-14	-27
2	0	3	10	10	30	21	-9
3	0	3	10	10	-15	-2	13
3	3	3	10	10	11	57	46
5	1	2	8	10	48	3	-45
3	2	3	10	10	22	2	-20
5	2	2	10	10	29	29	0
5	2	1	10	10	3	21	18
5	2	3	6	10	14	19	5
3	3	3	10	10	16	30	14
3	1	2	10	10	0	0	0
4	0	2	10	10	65	75	10
2	2	3	10	10	34	17	-17
4	1	1	10	10	15	11	-4
3	2	1	10	10	29	7	-22
3	3	4	10	10	75	54	-21

[a]Educational background.
[b]Exercise level.
[c]Number of risk factors.
[d]Pre-test score.
[e]Post-test score.
[f]Total blood cholesterol difference (visit 1 - visit 2).
[g]Total blood cholesterol difference (visit 1 - visit 3).
[h]Total blood cholesterol difference (visit 2 - visit 3).

Table XI:

Study Group Descriptive Statistics.

	N	Mean	Median	STDEV[g]	SEMEAN[h]	Min	Max
TBC1[a]	51	225.69	221.00	22.47	3.15	200	300
TBC2[b]	51	204.61	201.00	24.73	3.64	157	285
TBC3[c]	51	207.20	206.00	28.48	3.99	146	281
% Change[d]	51	9.04	7.66	9.76	1.37	-7.01	32.33
% Change[e]	51	7.94	5.37	11.34	1.59	-18.75	34.23
Age	51	36.43	31.00	13.37	1.87	20	60
Education background	51	3.51	3.00	0.93	0.13	2.0	5.0
Exercise level	51	1.57	2.00	0.96	0.14	0.0	3.0
# R.Fs[f]	51	2.61	3.00	1.10	0.15	1.0	6.0
Pre-test score	51	09.77	10.00	0.76	0.11	6.0	10.0
Post-test score	51	10.00	10.00	0.00	0.00	10.0	10.0

[a]Total blood cholesterol, Visit # 1.
[b]Total blood cholesterol, Visit # 2.
[c]Total blood cholesterol, Visit # 3.
[d]% Change = (a - b) X 100.
[e]% Change = (a - c) X 100.
[f]Number of risk factors.
[g]Standard Deviation.
[h]Standard Error of the Mean.

Table XII:

Comparison of Selected Descriptive Statistics of the Study, Normal, and Total Population Groups.

	N	M:F[1] Ratio	MEAN	MEDIAN	STDEV[2]	SEMEAN[3]	MIN	MAX
STUDY:	51	22:29						
1. TBC[4]			225.69	221.00	22.47	3.15	200	300
2. Age			36.43	31.00	13.37	1.64	20	60
3. R.F.[5]			2.61	3.00	1.10	0.15	1	6
Normal:	164	84:80						
1. TBC			163.80	167.00	23.30	1.82	100	199
2. Age			29.97	25.00	9.46	0.74	19	63
3. R.F.			1.35	1.00	0.80	0.06	0	3
Population	241	120:121						
1. TBC			184.34	181.00	38.78	2.50	100	300
2. Age			32.66	28.00	11.62	0.75	19	63
3. R.F.			1.77	2.00	1.07	0.07	0	6

[1]Sex distribution, Males:Females.
[2]Standard Deviation.
[3]Standard Error of the mean.
[4]Total blood cholesterol.
[5]Number of risk factors.

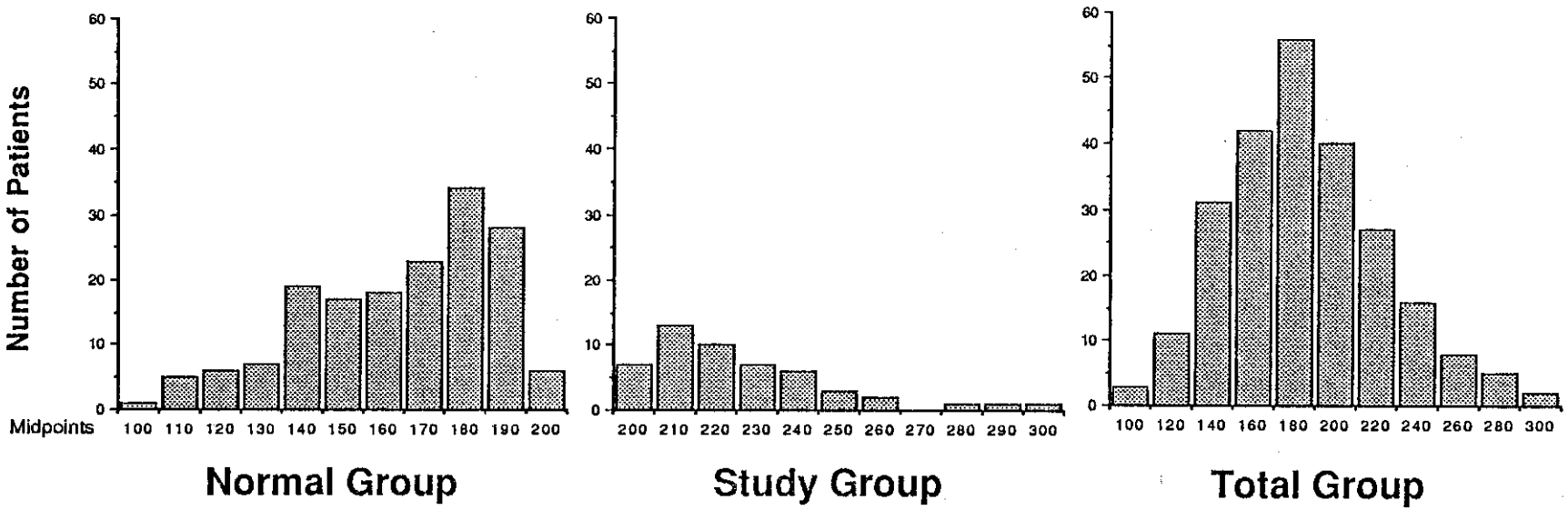


Figure 5: Histogram of Total Blood Cholesterol for the Normal Group, the Study Group, and the Total Population Group.

left portion represents people with normal TBC of <200 mg/dL.

As can be seen from Table XII, the study group patients tend to be significantly older compared to the normal group (means 36.43 and 29.97 years, respectively, $P< 0.05$). The median was found to be 31 for the study group, 25 for the normal group, and 28 for the total population. Examining Figure 6, it was decided to use 35 as the breakpoint to classify the study group into two subgroups, those who are under the age of 35 and the older patients whose age is 35-60 years old.

The sex distribution in the three groups tends to be equal, although more females were found in the study and total population groups than males (F:M ratio is 29:22 and 121:120 respectively). The normal population had less females than males (80:84) compared to the study group (29:22), although this difference is not statistically significant (calculated chi-square value =1.014, $P> 0.05$). This is a unique finding in this study because most clinical and epidemiological studies reported that coronary heart disease tends to occur 4-5 times more in males than in females. In fact, male sex, according the NCEP expert panel of 1987 and the Framingham study, is considered a risk factor for CHD.

When comparing the study group risk factors to those of the normal population, it was found that study group patients had a statistically significant higher risk for

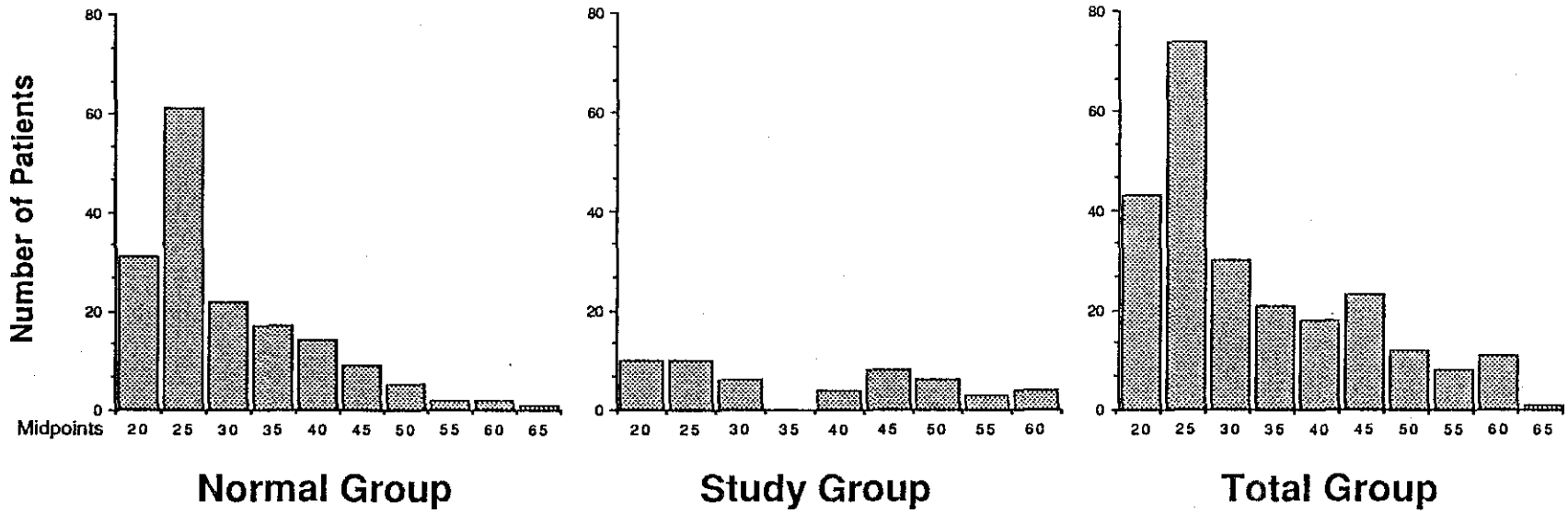


Figure 6: Histogram of Age for the Normal Group, the Study Group, and the Total Population Group.

CHD than those of the normal group (mean of 2.61 versus 1.35, P< 0.01). Since there is a possible argument that the study group may not represent an equally distributed sample, a non-parametric analysis was performed using the Mann-Whitney U test which is a non-parametric alternative to the two sample t-test. The non-parametric analysis of the number of risk factors between study and normal groups was also found to be statistically significant (P< 0.01). To assess the potential effect of the other risk factors, elevated TBC was temporarily excluded as a risk factor in the study group and statistical analysis was then performed. The difference between the study and the normal group was found to be no longer statistically significant (mean 1.61 versus 1.36 respectively, P= 0.12). This might confirm the association between elevated blood cholesterol as an independent factor for CHD. Table XIII summarizes statistical analysis results comparing the study group data against those data reported for the normal population group.

Study Group Comprehensive Analysis

The results reported in Table XI shows the mean reduction of TBC during the follow up visits (Visit 2 & 3). The maximum and minimum TBC levels were lowered from 200-300 mg/dL initially at visit 1 to 157-286 mg/dL in visit 2 and were lowered further at the end of study period, with visit 3 down to 146-281 mg/dL. This represents a percent change of -7.01 to 32.33% (-15 to 75 mg/dL) in visit 2 and

Table XIII:

Statistical Comparison of the Study Group Versus the Normal Population Group.

Parameter	N	Mean	T Value	P Value
TBC[1]				
-Study	51	225.7		
-Normal	164	163.8	17.03	P< 0.01
Age (years)				
-Study	51	36.40		
-Normal	164	29.97	3.21	P< 0.01
Sex[2]				
-Study	51		X^2=	
-Normal	164		1.01	P> 0.05
Number of Risk Factors				
-Study	51	2.61		
-Normal	164	1.35	7.61	P< 0.01
Number of Risk Factors Excluding TBC				
-Study	51	1.61	1.57	P= 0.12
-Normal	164	1.35		

[1]Total blood cholesterol, mg/dL.
[2]Based on Chi-Square statistics.

and a -18.75 to 34.23% (-39 to 76 mg/dL) in visit 3. Forty four patients (86.27%) in visit 2 and 35 patients in visit 3 of the study group stated that they changed their diet and/or improved their exercise as a result of the pharmacist's initial screening. Furthermore, 25 patients in visit 2 (49.02 %) and 22 patients in visit 3 (43.14%) showed a lowering in TBC level below the desirable 200 mg/dL cutoff point. In addition, 40 patients (78.43%) in visit 2 and 37 patients (72.55%) in visit 3 demonstrated a lowering in TBC below their baseline levels in visit 1 (Table X and Figure 7). On the other hand, only eight patients (15.69%) in visit 2 and nine patients (17.65%) in visit 3 had an increase in their TBC levels. It has been suggested that an expected 30-40 mg/dL reduction in TBC can be achieved over time by switching from the typical American diet to the step-one diet. An additional 15 mg/dL could be achieved by adhering to cholesterol-lowering diet as the patient advances to the step-two diet.[20]

The One-Way Analysis of Variance of the TBC on these three visits showed a statistically significant difference among the three groups, $P < 0.01$ (Table XIV). The Scheffe's test result showed a highly significant difference in mean TBC between visit 1 and 2 and between visit 1 and 3, $P < 0.01$. In contrast, no significant difference was found between mean TBC levels in visit 2 and 3, $P > 0.05$. This indicates that patients in the study group were able to lower their mean TBC within a one month period and

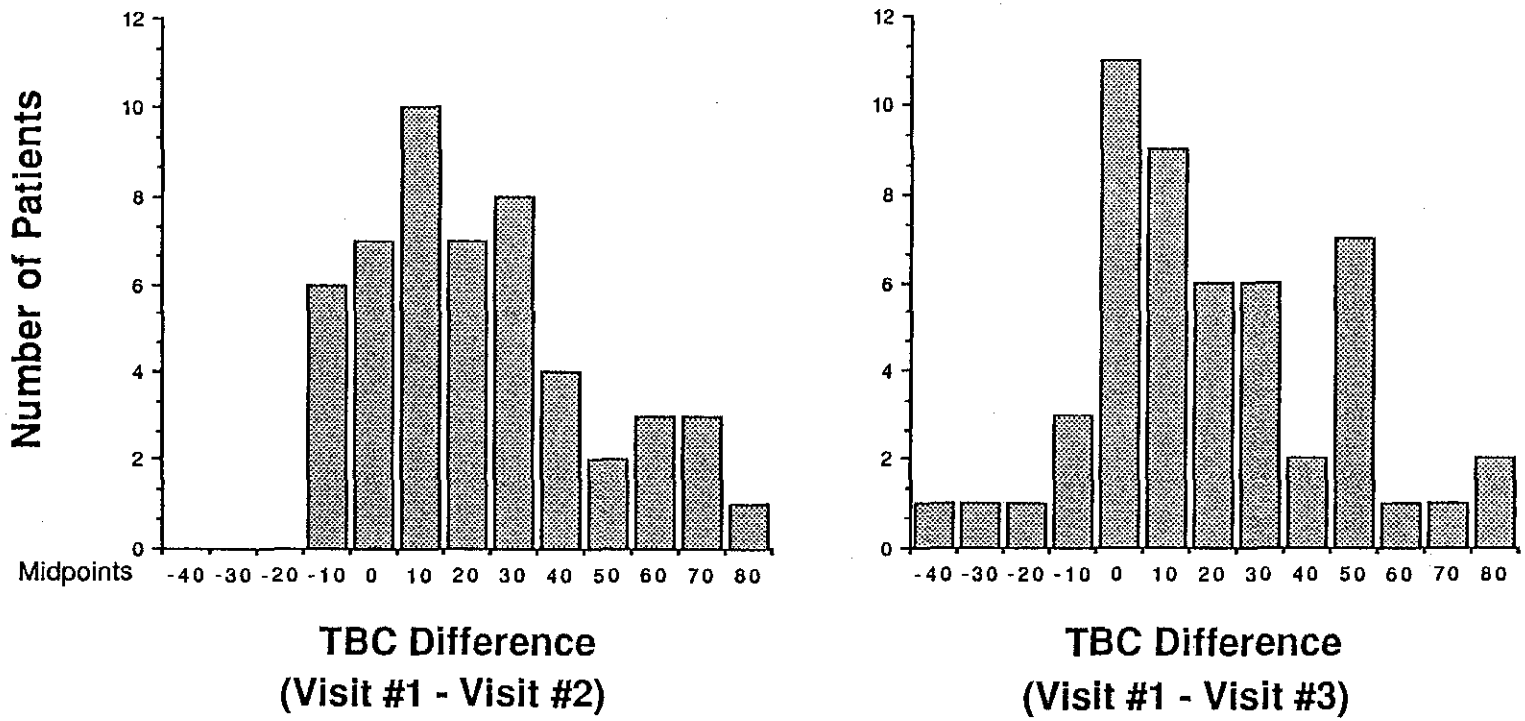


Figure 7: Histogram of the Study Group Total Blood Cholesterol (TBC) Difference Between (Visit #1 - Visit #2) and Between (Visit #1 - Visit #3)

Table XIV:

One-Way Analysis of Variance of Total Blood Cholesterol in the Three Visits.[a]

	Mean total Blood Cholesterol (mg/dL)	F Ratio	P Value
Visit 1	225.69		
Visit 2	204.61	10.49	<0.01
Visit 3	207.20		

[a]Scheffe Value: Significant difference between visit 1 and 2 and between Visit 1 and 3, ($P< 0.01$). No significant difference between visit 2 and 3, ($P> 0.05$).

succeeded in keeping it at a significantly lower level compared to their mean initial cholesterol level. Additionally, this might emphasize the need for early follow up procedures to assure patient compliance with prescribed diet or drug treatment especially for long-term management of elevated blood cholesterol.

Six patients on the first follow up test (visit 2), four at high risk and two at moderate risk of CHD, reported that they contacted their physician as a result of the initial screening to establish their diagnosis. In addition, two more patients at high risk and another patient at moderate risk reported that they had seen their physician during the time interval between visit 2 and visit 3. It is important to note here that standard laboratory lipid analyses had been ordered for these nine patients by their physicians. Table XV shows that hypercholesterolemia was confirmed in all patients (N=9) referred with the exception of one patient who successfully lowered her TBC below 200 mg/dL. This patient had reported standard laboratory TBC result of 181 mg/dL on April 25,1988, which was found to be 177 mg/dL in May 4, 1988 using the project analyzer "Reflotron".

There was a "very good" association between standard laboratory results compared to that performed in the community pharmacy project. The difference in both TBC reported (Table XV) in those nine patients was not statistically different from the results reported fort the

Table XV:

Comparison of Two Reflotron Results Against Those Obtained at Standard Laboratories.[a]

Study Codes	Results Confirmed	Reflotron		Standard Labs.	
		TBC[b] (md/dL)	Test date	TBC (mg/dL)	Test date
04	Yes	289 ; 285	03/23;05/02	252	04/03/88
08	Yes	221 ; 229	03/23;06/02	235	06/21/88
09	Yes	216 ; 177	03/29;05/04	181	04/25/88
10	Yes	252 ; 227	03/30;05/03	251	04/20/88
24	Yes	241 ; 231	04/08;05/10	214	06/16/88
36	Yes	229 ; 216	04/18;05/19	272[c]	04/25/88
37	Yes	257 ; 227	04/18;05/19	277[c]	04/20/88
40	Yes	284 ; 236	04/19;05/25	277	04/26/88
47	Yes	300 ; 235	04/25;06/17	275	06/03/88
Additional Out of the Study Comparison Data:[d]					
Volunteer Number:	1	188	04/12/88	189	04/12/88
	2	178	07/01/88	168	07/01/88
	3	160	04/21/88	177	02/11/87
	4	217	04/15/88	223	12/15/87
	5	230	09/16/88	240	09/16/88

[a]No statistical significant difference (P= 0.69 and P= 0.21).
[b]TBC= Total blood cholesterol.
[c]Delta Medical Laboratory.
[d]No statistical significant difference (P= 0.81).

same nine patients by standard laboratories (means 254.3 versus 248.2 mg/dL, P= 0.69 for TBC initial levels and 229.2 versus 248.2, P= 0.21 during visit 2 and 3). Additionally, a group of five volunteers who had their total blood cholesterol measured at standard laboratories were tested in this community pharmacy project to compare the laboratories' results to that of the Reflotron. Again, the difference between these project's results and those of standard laboratories were found statistically insignificant (study group mean of 194.6 versus 199.4 for the standard laboratories, P= 0.81). This was found to be in accord with the reported accuracy and precision of the Reflotron analyzer.[76,77,80,81] On the other hand, the presence of inter-laboratory variation in TBC measurement was confined to only one laboratory. This laboratory reported relatively high values compared to those obtained during the community pharmacy screening tests (patient #36 & #37 in Table XV). This problem of variation of serum cholesterol determination from one laboratory to another has been addressed in the literature.[76,79] For this reason the National Committee for Clinical Laboratory Standards (NCCLS) through its council has approved the National Bureau of Standards (NBS) definitive method and the Center for Disease Control (CDC) reference method and their certified reference materials as the accuracy base for serum cholesterol measurement in the United States. The CDC in a special report[76] stated that "The utilization of

the National Reference system for cholesterol will assist the organized national effort to assure and monitor reliable cholesterol determination in the laboratories." Therefore, users need to know the limitation and the percent bias of the new simple-to-operate desk-top analyzers before adopting them for routine patient use.

Data on the patients' educational background (which reflects the number of years of education) were collected to investigate its effect on patients' initial TBC and subsequent behavior changes and their effect on the final cholesterol levels. Educational background was assessed using a scale from 1 (Grade School) to 5 (Postgraduate degree) as can be seen in Appendix B. None of the study group patients had an educational background below high school level (level 2). The average educational background level of the study group was 3.51 (range 2-5), an education above the undergraduate level. Therefore, they would be expected to have a relatively high pre-test score and even higher post-score results. As expected, the pre-test score ranges from 60-100% while all post-score test were at 100%, a statistically significant difference at $P< 0.05$.

To evaluate the influence of the number of years of education on final blood cholesterol, a One-Way Analysis of Variance was performed to compare TBC of the four educational levels in visit 2 and 3 to that at visit #1 (initial screening test). As shown in Table XVI, the calculated F-values were 0.41, 0.98, and 1.34 for visit 1,

2, and 3 respectively, whereas F-table value was found to be 2.8. It is concluded that there was no statistically significant difference in terms of TBC changes during the three visits between the investigated four educational background levels. It is worth noting that patients in the four educational levels had successfully lowered their mean TBC levels in visit 2 and 3 compared to their initial mean levels. However, patients with high school level and the postgraduate degree patients did worse in visit 3 compared to visit 2, though still less than their initial mean levels.

Investigating the role of sex in lowering TBC, a two sample t-test was performed comparing male versus female mean TBC levels at the three visits. It was found that there were no significant differences in mean TBC levels between males and females in visit 1, 2, or 3 (calculated T-values are 0.12, 0.21, 1.41 respectively; T-table 50, alpha=0.05 is 1.65). Mean total blood cholesterol (TBC) of males decreased from 226.3 in visit 1 to 205.0 in visit 2 and even lower at 201.0 at the end of the study period (visit 3). On the other hand, mean TBC of females decreased from 225.5 mg/dL in visit 1 to 203.6 in visit 2, but increased again to 212.2 mg/dL in visit 3. It is documented that as people get older their TBC tends to increase to a certain degree. Therefore, we investigated the effect of age on TBC by assigning all study group patients 35 years of age and under to subgroup 1 and those

Table XVI:

One-Way Analysis of Variance of Effect of Educational Background on Blood Cholesterol.

Variable	Education Background Level[a]				F	P
	level2	level3	level4	level5	Ratio	Value
Visit 1	232.60	223.36	223.55	230.40	0.41	NS[b]
Visit 2	196.20	200.88	207.91	214.50	0.98	NS
Visit 3	213.00	201.32	204.73	221.70	1.34	NS

[a]Levels 2, 3, 4, and 5 represent high school, undergraduate student, undergraduate degree, and postgraduate degree classes respectively.

[b]NS = Non-Significant difference.

of 36-60 years old to subgroup 2. The study patients were also categorized to two subgroups based on their TBC by coding their TBC into either subgroup 1=TBC of 100-199 mg/dL and subgroup 2=TBC of 200-300 mg/dL. Using this coding system for TBC and age, there was no statistically significant difference between younger patients (<35 years old) and older patients (36-60 years old) in terms of TBC in visit 1 (mean of 224.8 and 226.6 mg/dL respectively, P= 0.78). In contrast younger patients did significantly better in terms of lowering their initial TBC than older patients in visit #2 and maintained this difference to the end of the study period (means 197.1 Vs. 212.4, P= 0.025 in visit 2, and 197.5 Vs. 217.3 in visit 3). When the difference in mean TBC between (Visit 1 - Visit 2) and (visit 1 - visit 3) was compared in terms of age code, younger patients had significantly higher mean TBC differences in visit 2 and 3 compared to visit 1 (mean lower TBC is 27.7 Vs. 14.2 mg/dL between visit 1 and visit 2, P< 0.05 and 27.3 Vs. 9.3 mg/dL between visit 1 and 3, P< 0.05. This might indicate that younger people are relatively easier to motivate to lower their TBC and to change their lifestyle than older people. If this was assumed to be the case, it seems prudent to start screening adult individuals 20 years and older or perhaps earlier in the presence of strong family history of CHD. Early detection and management of elevated TBC and assessment of underlying risk factors may be of potential value in

halting or even reversing the process of fatty streak build up and the development of atherosclerosis and CHD.

A correlation matrix of TBC for the three visits, difference and percent changes in TBC during these visits, study group age, education level, exercise level, number of risk factors, pre- and post-test scores, was performed. There was no strong correlation between any of these parameters ($r > 0.90$ or higher). However, several positive correlations were found between TBC in visit 1 and that of visit 2 and 3 and between visit 2 and 3 ($r = .515$, 0.510, and 0.537, respectively). In addition, positive correlations were found between age and TBC in visit 2 and 3 ($r = 0.29$ and 0.36), number of risk factors and TBC in visit 1, 2, and 3 ($r = 0.37$, 0.32, and 0.26). On the other hand, exercise level of the study group patients was negatively correlated with TBC in the three visits, although the correlation was weak ($r = -0.436$, -0.451, and -0.316). It is important to note that although TBC and hypertension, for example, are both independent and strong predictor risk factors of CHD, their correlation coefficient was reported to be 0.12 indicating weak correlation.[10,13,67] Nevertheless, it was found in the same Framingham study that the increase in blood pressure paralleled the increase in total blood cholesterol. Thus, in hypertensive individuals, blood cholesterol related to CHD risk was found to be strong and graded from level 182 mg/dL and higher and not restricted to the 75th and 90th

percentile.[9,68] Furthermore, it should be remembered that CHD is a multifactorial health problem and not a disease of a single etiology. No one risk factor for CHD is a rigorous determinant by itself because the risk associated with any single factor varies with the constellation of other existing factors. Accordingly, multiple intervention should be targeted to lower elevated blood cholesterol and blood pressure, decrease the number of cigarettes smoked, and control elevated blood sugar. Also, lowering fat and cholesterol consumption and maintaining ideal body weight, screening for secondary hyperlipidemia including medications that might affect blood cholesterol or blood pressure, and other outlined lifestyle modification all contribute to lowering the incidence of CHD morbidity and ultimate mortality.

Table XVII lists the study group patients on chronic medication, the number of drugs and their therapeutic categories used per patient. Thirteen patients (25.49%) of the study group use medications on a chronic basis (mean usage of 1.85 drugs/person). As expected, approximately 85% of these patients are above the age of 40 years. In the 20 year old patient (#9), rheumatoid arthritis was incorrectly diagnosed and the patient reported at the end of the study period that she was no longer taking her medication in light of the new diagnosis. The other 23 year old patient is taking minocycline for treating acne, in addition to her birth control pills, indicating no

Table XVII:

Study Group Patients on Chronic Medications.

Code	Age	TBC1[a]	TBC2	TBC3	# of Meds	List of Drugs
04	40	289	285	273	3	Diabeta/Lasix/ Synthroid
07	52	219	227	237	2	Premarin/Synthroid
09	20	216	177	181	1	Clinoril
11	52	210	199	210	2	Premarin/Provera
13	60	202	202	211	2	Seldane/Provera
17	23	207	172	206	2	Minocycline/BCP[b]
19	60	204	203	204	1	Atarax
31	58	217	201	192	2	Estrogen/Synthroid
36	52	229	216	243	2	Moduretic/Premarin
37	60	258	227	236	4	L-Thyroid/Premarin/ Inderal and Dyazide
40	56	284	236	281	1	Estrogen
46	43	215	215	215	1	Synthroid
49	45	12	197	201	1	Estrogen Patch

[a]TBC = Total blood cholesterol.
[b]BCP = Birth control pills.

underlying severe disease condition. The effects of medications used by the rest of eleven patients on blood cholesterol level were explained on an individual basis and patients were advised to communicate the information with their physician.

Attitude Toward the Feasibility and Future Implementation of Blood Screening in Community Pharmacies

During the final cholesterol test (visit 3) all patients were asked to complete a questionnaire by circling the appropriate answer indicating agreement or disagreement with the statements. The subject's willingness to pay a reasonable fee for this service if it were available in their community pharmacy was also investigated. Suggested fee levels were provided to each patient, namely, $3 or less, $5, $10, and more than $10 (See questions 11-14, Appendix G). Ninety eight percent (50 of 51) of the 51 study patients stated that they strongly liked the idea of screening blood cholesterol in community pharmacies. One person showed moderate acceptance of this idea. All study group subjects agreed that providing this proposed community service would be very convenient for them. Forty seven patients (92.16%) showed a willingness to pay for this service if it were available in a community pharmacy. Only four patients (7.84%) reported they were unwilling to pay for this service. When asked about the reason for not paying for the services, some stated that unless they have medical problems, or had a strong family or personal history of CHD, they would not have their blood level tested. In others, they suggested that University of the Pacific should pay for this service during the initial student enrollment or as an ongoing service as a part of the University Health Center services. For those who

showed a willingness to pay, an average of $4.55 was proposed as a reasonable fee to charge for this service (Range $3 to $10). Keeping in mind that this project was conducted in an academic environment, where most of project's participants are students, most participants circled $3 or less. Further, since this was an experimental service not covered by conventional health insurance, many would be reluctant to endorse it as a high cost service. However, with more widespread and effective marketing of this service, it may be financially feasible to provide it at low cost to the public.

When subjects were asked to identify which of the eight available tests they would use in the future, cholesterol (98.0%) and triglycerides (62.7%) were the two most desirable tests. This might be the result of intensive media coverage of the CHD/cholesterol issue during the period of this research project. In fact, April 1988 was chosen as the "Know Your Cholesterol" month in an effort to motivate everyone to know his/her cholesterol level. Table XVIII reports the number and percentage of patients who indicated interest in future utilization of blood tests if available. In a five-week study[99], 443 subjects completed a pharmacy blood service questionnaire involving blood level list of nine blood tests. Cholesterol and potassium were reported to be the tests subjects showed most interest in their availability in a community pharmacy (72.7% and 70.01% respectively), while triglycerides came fifth next

Table XVIII:

Subjects Interest in Future Blood Level Measurement in Community Pharmacy.

Tests Available	Number of Subjects	%
Cholesterol	50	98.0
Triglycerides	32	62.7
Hemoglobin	16	31.4
Glucose	24	47.1
Uric Acid	12	23.5
Serum Creatinine	16	31.4
Blood Urea Nitrogen	12	54.9
Liver Function Tests (GGT, SGOT, SGPT)	19	37.3

to glucose and hemoglobin (49.9%).

Table XIX shows the number of patients in the study group whose TBC increased during visit 2 and 3, and corresponding behavior changes. Nine out of the listed 13 patients in visit 2, and 12 of the 13 patients in visit 3 showed a matching result that corresponds to their behavior change.

Table XIX:

Behavior Changes Versus Increased Cholesterol at Visit 2 and Visit 3.

Code[a]	Age	Visit 1	Visit 2	Visit 3	Diet/Exercise Changes		Did TBC[b] Decreased?	
					V2[c]	V3[d]	V2	V3
02	45	235	237	224	NO	YES	NO	YES
03	40	222	235	211	YES	YES	NO	YES
07	52	219	227	237	NO	NO	NO	NO
13	60	202	202	221	NO	NO	YES	NO
14	48	251	221	266	YES	NO	YES	NO
16	46	208	213	247	YES	YES	NO	NO
18	24	223	232	215	YES	YES	NO	YES
23	23	200	176	234	YES	NO	YES	NO
25	22	238	171	240	YES	NO	YES	NO
32	22	204	217	204	NO	YES	NO	YES
34	54	227	236	230	NO	NO	NO	NO
36	52	229	216	243	YES	NO	YES	NO
38	21	214	229	216	NO	NO	NO	NO

[a]Code number of patients in the study group whose cholesterol increased during Visit 2 and Visit 3.
[b]Total blood cholesterol.
[c]Visit 2.
[d]Visit 3.

SUMMARY AND CONCLUSION

This research project was undertaken to investigate the feasibility of conducting a cholesterol screening program in a community pharmacy. It was targeted toward identifying individuals with high blood cholesterol levels and those at high risk of coronary heart disease (CHD). Since CHD is usually a silent and slowly progressive disease that presents no early clinical symptoms, it was theorized that early detection of those at risk could advance the time of their diagnosis and hence enhance their prognostic value. Early detection and management of patients with hypercholesterolemia and those at CHD risk through screening programs would help eliminate or control these risk factors by taking preventive measures early before progression of the disease.

In the 51 patients of the study group, there was a statistically significant reduction in mean total blood cholesterol (TBC) levels in visit 2 and 3 compared with the initial mean level ($P< 0.01$). The mean percent changes in TBC between visit 1 and 2 was 9.04% (range -7.01 to 32.33%) and 7.94% (range -18.75 to 34.23%) between visit 1 and 3. Furthermore, 25 patients (49.02%) in visit 2 and 22 patients (43.14%) in visit 3 had successfully reduced their TBC to the recommended level (less than 200 mg/dL). Compared with the mean baseline TBC level, 41 patients (81.39%) and 37 patients (72.55%) had a decline in TBC in

visit 2 and visit 3, respectively. The study group patients were found to have a significantly higher number of risk factors compared to those of normal population group, $P< 0.01$. The drop out rate was found to be 10.53% (six patients) throughout the six month study period (as compared with a drop out rate of 27.7% after two months in a multi-site screening program).[94] No age, sex, or educational background differences in terms of mean TBC levels were found during the initial TBC testing. However, young patients (less than 35 years old) significantly lowered their mean TBC levels compared with older patients (35-60 years old), $P< 0.05$). No difference in mean TBC was found between male and female patients in visit 2 or 3 although both males and females were able to lower their mean TBC levels in these two visits. Similarly, there was no significant difference between the investigated educational background levels in terms of mean TBC levels during the two follow up visits (visit 2 and 3). Analysis of patient attitudes toward the model showed a positive acceptance.

It is concluded that cholesterol screening in this community pharmacy was effective, acceptable, and may prove to be financially feasible if effectively planned. The concept of cholesterol testing and follow up should be tested in other non-academic setting to validate the findings of this study. It is expected that younger individuals (20 years old and above), those at high risk of

developing CHD, and patients on medication to lower TBC will benefit most from such service.

Appendix A

Consent Form
Cholesterol Screening Project

You are being asked if you wish to take part in a cholesterol screening project. Please read this consent form carefully and ask as many questions as you like before deciding whether you want to participate. If you decide to participate in this study, you will have a finger stick performed by a pharmacist in order to collect the necessary blood sample for the test. Finger sticks are accompanied by minor discomfort at the site of the finger puncture and may result in slight bruising at the site. Approximately three drops of blood will be collected. The time required for this procedure should be less than five minutes. If your cholesterol level is over 200, you will be requested to appear for two follow-up visits. The screening test we will use may overestimate true levels.

The benefit you can expect from this study is the knowledge of your cholesterol level and whether or not you should receive further evaluation by your physician. Elevated blood cholesterol is known to be directly correlated with a high incidence of coronary artery disease which, if undetected and untreated, may lead to atherosclerosis and heart attack. The duration of your participating in this study is the time required for finger stick, blood collection and analysis, and answering the awareness survey provided.

At the time of this initial screening, you will be given a copy of the results for your records and a copy will be forwarded to your physician, unless you indicate otherwise. Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission. The sponsor of this project will receive summaries of the study. Also, you will be required to complete forms regarding your health.

If you have any questions, please ask. If you have any additional questions later, please contact your pharmacist Osama Ibrahim, M.S. at (209) 946-2440, your Campus Pharmacy manager Joel Wagner, Pharm.D. at (209) 946-2411 or the project coordinator Dr. Patrick Catania at (209) 946-2491.

Your signature indicates that you have read the information provided and have had your questions answered and have decided to participate.

I, _____, freely give my consent to take part in this study. I will receive a copy of this consent form for future reference. I have been advised that the University of the Pacific has no special program by which it provides compensation of medical treatment if injury occurs during biomedical or behavioral research.

_____ _____
Signature of Participant Date

_____ _____
Signature of Investigator Date

Your blood cholesterol reading is _____mg/dl Date: / /1988
Would you like a written screening result to be sent to your physician or health center? Yes No

Appendix A (Cont.)

Boehringer Mannheim Diagnostic Consent Form

Cholesterol Screening Consent and Release Statement

I hereby release Boehringer Mannheim Corporation, other organizations associated with this screening, parent and affiliated companies, successors and assigns, and officers, directors and employees from any and all liability arising from or in any way connected with blood drawing for my blood cholesterol measurement or from the data derived therefrom. I understand that:

1) The data derived from this test are to be considered preliminary only and do not constitute a diagnosis of hypercholesterolemia.
2) With my permission, screening sponsors may elect to send the results of this test to a physician of my choice if my results suggest that I may be at increased risk for heart disease according to the National Institutes of Health guidelines.
3) Boehringer Mannheim Corporation will also receive a copy of this completed form, including test results, for research purposes only.
4) The responsibility for initiating a follow-up examination to confirm high blood cholesterol and obtain advice and treatment is mine and not that of my physician or the organizations associated with this screening.

Signature _____ Date _____

BOEHRINGER MANNHEIM DIAGNOSTICS
9115 Hague Road, Indianapolis, IN 46250

Appendix B

University of the Pacific
School of Pharmacy
Cholesterol Screening Project

CHOLESTEROL DATA SHEET

Date: / / 1988

Name:_____ Telephone number:( ) -
(Last) (First) (Mid)
Date of birth: / / Sex: M F Height: ' " Weight:

Family Physician:

Please, answer the following questions:

1. Do you smoke? No____ Yes____ How many cigarettes/day: _____

2. Are you taking Birth Control Pills? Yes____ No____

3. Are you a diabetic (high blood sugar)? Yes____ No____ I don't know____

4. What is your blood pressure? ____/____ I don't know_____

5. What is your exercise level? ____ Active (at least 1/2 hour every day)
____ Moderate (at least 1/2 h every other day)
____ Mild (Weekends only)
____ Not active (less than once a week)

6. Does any person in your family have a history of heart problems, e.g., chest pain, hypertension, or heart attack: Yes____ No___ I don't know___

7. Do you have abnormal thyroid function? Yes____ No___ I don't know___

8. What is your educational level?
_____ Grade school
_____ High school
_____ Undergraduate student
_____ Undergraduate Degree (B.A./Pharm.D.)
_____ Postgraduate degree (M.S./ Ph.D.)
_____ Not stated.

9. Are you currently following a special diet,e.g., lowfat/weight control diet)?
No ____
Yes____
If yes, specify:_____

10. Are you taking prescription medication on chronic basis?
No_____ Yes_____, How many: 1 2 3 4 5

Please, Do not write below this line

IBW =	Kg	Ob:
# R. F.:		
* * CHOLESTEROL =	mg/dL	GN: N B H

Appendix C

Cholesterol Awareness Survey (Pre-test)

University of the Pacific
School of Pharmacy
Cholesterol Screening Project

Please circle the appropriate answer according to your best knowledge.

1. Have you ever heard of high blood cholesterol or hyperlipidemia? Yes No
2. Have you ever had your blood cholesterol checked? Yes No
3. Have you been told by a doctor that your blood cholesterol is high? Yes No
4. High blood cholesterol is affected by dietary factors. True False
5. Does high cholesterol lead to hardening of the blood vessels (arteries)? Yes No
6. Does high blood cholesterol lead to heart attack ? Yes No
7. Do you think that dietary action such as eating less saturated fats, egg, and lard would lower blood cholesterol? Yes No
8. Do you believe that reducing elevated blood cholesterol will have a large effect on heart disease? Yes No
9. If you were found to have elevated blood cholesterol, would you be willing to make dietary changes and/or take medication to lower your blood level?
   ___Yes ___No ___I'am not sure
10. Cigarette smoking by itself will increase your risk of heart attack?
    ____True ____False

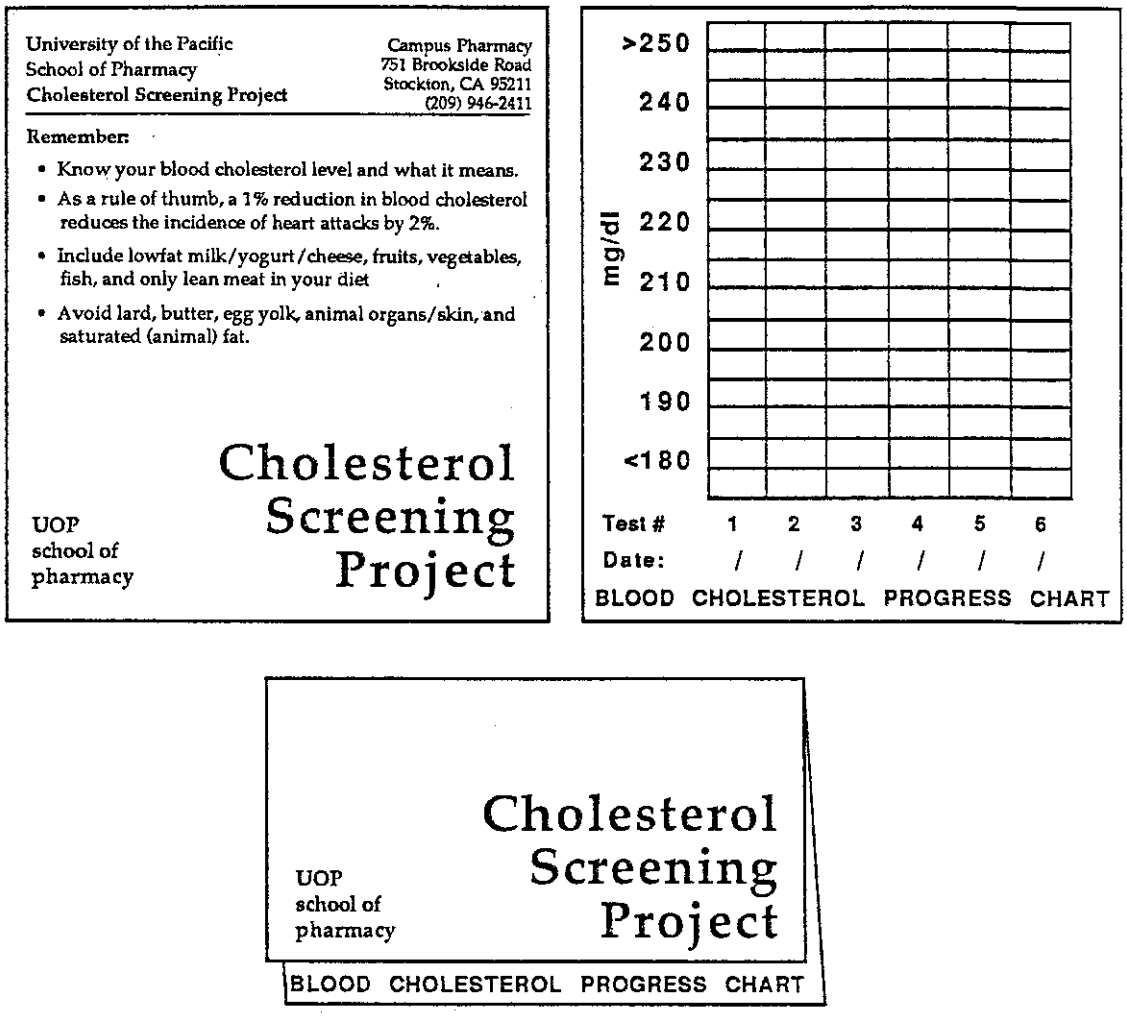
Appendix D

PATIENT EDUCATION MATERIAL
USED IN THE STUDY

Name of Publication	Source
1. Combat High Cholesterol	Citizens for Public Action on Cholesterol
2. Coronary Risk Factors	American Heart Association
3. Exercise and Your Heart	American Heart Association
4. Your Heart and Dyslipidemia (It's more than High cholesterol)	Park-Davis
5. Elevated Cholesterol	Merk Sharp & Dohme
6. Lowering Your Cholesterol (Diet information guidelines)	Merk Sharp & Dohme
7. Cholesterol, Questran and You	Bristol Laboratories

Appendix E

Blood Cholesterol Progress Wallet Card



Appendix F

Preliminary Evaluation Sheet

University of the Pacific
School of Pharmacy
Cholesterol Screening Project

If you were found to have a high blood cholesterol level would you be willing to:

1. Voluntarily modify your diet in an attempt to lower your elevated cholesterol by eating less saturated fats and cholesterol for a one month trial period. Yes No

2. Repeat your blood cholesterol analysis twice by your pharmacist within a 4 month period (one and three months after this initial test) absolutely FREE. Yes No

3. Receive appropriate educational material, a pharmacist's advice, and answers to your questions on cholesterol. Yes No

4. Be referred to your family physician or a health center to establish the final diagnosis of your condition. Yes No

5. Give authorization to your pharmacist to receive a copy of your blood lipid profile for follow-up purposes. Yes No

6. Receive a certificate of participation in our project. Yes No

Participant's Signature _____ Date _____

Appendix G

Participant Interest in Future Blood Level Measurements

From the following list, please circle the number of test(s) which you would use in the future if they were available in your community pharmacy:

#	Tests Available
1	Cholesterol
2	Triglycerides
3	Hemoglobin
4	Glucose
5	Uric Acid
6	Serum Creatinine
7	Blood Urea Nitrogen
8	Liver Function Tests (GGT, SGOT, SGPT)

Appendix H

Cholesterol Awareness Survey (Post-test)

University of the Pacific
School of Pharmacy
Cholesterol Screening Project

Please circle the appropriate answer:

1. High blood cholesterol is affected by dietary factors. **True False**

2. Which of the following contains the **highest** amount of **cholesterol**?
   a-Egg white (1 large) b-Butter (1 tsp) c-Liver, beef (2 oz) d-Sea food & fish (2 oz)

3. Which of the following contains the **highest** amount of **saturated fats**?
   a-2 % milk (1 cup) b-Low fat yogurt (8 oz) c-Coconut oil (1 tbsp) d-Shrimp,steamed (2 oz)

4. Which of the following contains **low cholesterol** content but **high in saturated fat**?
   a- popcorn (buttered) (2 oz) b-Apple (one) c-Coconut oil (1 tbsp) d-Skim milk (1 cup)

5. Does high cholesterol lead to hardening of the blood vessels (arteries)? **Yes No**

6. Does high blood cholesterol lead to heart attack ? **Yes No**

7. Do you think that dietary action such as eating less saturated fats, egg, and lard would lower blood cholesterol? **Yes No**

8. Do you believe that reducing elevated blood cholesterol will have an effect on heart disease? **Yes No**

9. Because of your elevated blood cholesterol, did you make dietary changes and/or take medication to lower your blood cholesterol during this study? **Yes No**

10. Did you consult with other health care provider (your physician, health center, or a dietition to reduce your blood cholesterol as a result of the screening project?
    No I will Yes: specify _____

11. What is your attitude toward the idea of screening blood cholesterol in a community pharmacy done by a pharmacist?

    a. I strongly like it b. Moderately like it c. I don't like it

12. Is it a convenient service for you? **Yes No**

13. If blood cholesterol analysis were available in your community pharmacy, would you use this service in the future? **Yes No**

14. Would you be willing to pay for this service if it were to be offered in your neighborhood pharmacy?
    No Yes: If so, what would be a reasonable fee?
    $3 or less **$5** **$10** More than **$10**

Appendix I

University of the Pacific
School of Pharmacy

CERTIFICATE OF PARTICIPATION

This certifies that

_____

has successfully participated in
The Pharmacist's Cholesterol Screening/Awareness Project
conducted at the School of Pharmacy.
This is a recognition of the participant's effort to lower coronary artery disease mortality and morbidity and to keep America healthy.

Dated this _____ day of _____ 1988

_____
Osama M. Ibrahim, M.S.
Project Investigator

_____
Joel A. Wagner, Pharm.D.
Campus Pharmacy Manager

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